



Applikon Biotechnology, a step ahead

Applikon Biotechnology is a world leader in developing and supplying advanced bioreactor systems from laboratory scale to production scale. We partner with our customers to implement scalable platforms from initial screening through development and full-scale production. This minimizes scale-up risks and guarantees the shortest time to market for our customers' new product development.

New technologies

Applikon is known for bringing new technologies to the market. These new technologies offer advantages in process efficiency for research and development as well as pilot plant and production scale processes. Your advantage? Working with the latest technology offering a competitive advantage in efficiency and reliability.

Reliable

As a privately owned company our focus is on building a healthy company by supplying the best product offering for our customers now and in the long-term future. This is the basis of many long-term relationships with our clients all over the world.

Your advantage? Applikon can always support you through the well trained sales consultants and technicians of our technical support department.

High Tech

Applikon Biotechnology is unique in the mini and micro bioreactor range. No other company can offer this complete solution on a very small scale. We develop small scale systems to generate results that can be scaled to production scale. There are thousands of Applikon bioreactors used in the world from small scale R&D up to full scale cGMP production.

Your advantage? The best solution from micro scale to full scale production resulting in the shortest time to market for your new products.

Worldwide activities

Since we started in 1974 we have shown a healthy growth resulting in a global market leader role. R&D, design and engineering are in house in our headquarters in Delft, The Netherlands. We have our own sales and service organizations in the USA, the UK and China. We have well trained local distributors for sales and service in over

Your advantage? No matter where you are you can always rely on Applikon, now and in the future.

Our Mission

Providing reliable solutions for the bioprocess market that will enable an improved quality of life.



RAMbio,® the high intensity mixer

The RAMbio® bench top biological mixer utilizes ResonantAcoustic® technology that applies low-frequency, high-intensity acoustic energy to agitate microbial cultures. The RAMbio® is a highly-efficient mixer/incubator that dramatically enhances oxygenation and bulk mixing for bacterial and fungal cultures. Combined with the patented Oxy-Pump® stopper, oxygen transfer rates up to 6-fold higher than orbital-shaken cultures can be achieved.

Features

- Increased oxygen transfer for aerobic cultures
- Rapid turnover of any desired gas
- Take advantage of richer media formulations
- 2-6 fold increase in plateau biomass levels
- Up to 10-fold increase in product expression
- Up to 6-fold increase in Oxygen Transfer Rate
- Up to 5 times shorter cultivation time
- Humidity control







Shake flask under the influence of ResonantAcoustics®



Capacity	18 x 250 ml flasks or
	14 x 500 ml flasks or
	8 x 1000 ml flasks
Dimensions	102 x 57 x 70 cm (W/D/H)
	40 x 27 x 23"
Temperature control	Ambient +5°C to 60°C
Weight	200 kg (440 lbs)
Humidity control	Ambient to 90% RH
Power	110/230 VAC, 50/60 Hz
Mixing power	3 - 20g acceleration (196 m/sec²)

Anaerobic Fermentation Monitor, simple parallel cultivation

The Anaerobic Fermentation Monitor (or AFM) is a robust and user-friendly laboratory parallel fermentation system that allows for accurate comparisons of carbon conversion rates and yields for six simultaneous anaerobic fermentations.

Monitoring the amount of gas that evolves from a fermentation broth under well controlled conditions is a reliable comparison method that has proven to be very useful in all industries that use anaerobic fermentations. Because carbon dioxide production is stoichiometrically coupled with carbon source conversion, very useful metabolic data can be obtained.

The AFM provides very accurate standard measuring of gas from six parallel fermentations that is both very low in maintenance and very easy to use.

Features

- Very user friendly laboratory device for monitoring anaerobic, metabolic yeast activity for alcohol production
- Six independent yeast fermentations can be carried out simultaneously
- Stirrer speeds and temperatures can be set or time programmed for each fermenter flask individually
- · Accurate comparison of conversion rates and yields under different conditions such as temperature, strain type, carbon source or nutrients
- Much easier to operate and cleaner than standard fermenter systems
- Fully controlled with user-friendly PC control and data analysis software
- Automatic generation of advanced reports containing all measured data, data analysis tables and corresponding graphs
- Very strong magnetic stirrers, able to handle very viscous media
- Proven value for research and QA purposes in all fields of yeast research and (bio) ethanol production



- · Measure conversion rates and yields of lignocellulose hydrolysates into biofuels
- Test and compare different yeast strains or different feedstock/substrates
- Quality control of regular/commercial yeast
- · Quality control of traditional feedstock (such as molasses)
- Conversion of wort into beer
- · Conversion of grape juice into wine
- Alcohol tolerance and toxicity studies
- Industrial and academic research on yeast and potable alcohol/bio-ethanol/bio-butanol production

Total volume (liter)	6 reactors of 250 ml or 500 ml
Working volume (liter)	200 ml or 400 ml
Minimum working volume (liter)	50 ml or 100 ml
Drive system	Magnetically coupled drive
Maximum stirrerspeed (rpm)	Standard range is 50 - 500
Impellers	Marine type
Exhaust gas	Exhaust gas connection
Temperature	Measurement: Pt-100 sensor in central stirrer bar
	Control: heating via central stirrer bar
Dimensions (DxWxH)	30 x 85 x 67 (cm)
Empty Weight (kg)	75 kg



Micro-Flask by Duetz, cultivation in microtiter plates

The Micro-Flask system facilitates reproducible and reliable culturing on microtiter plates.

The system consists of sandwich covers, cover clamps and cryo-replicator.

The Micro-Flask enables a single person to grow and test thousands of strains simultaneously with a minimum of repetitive handling.

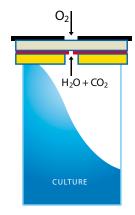


Cryo-Replicator for simple inoculation of 96-well microtiter plates

Features

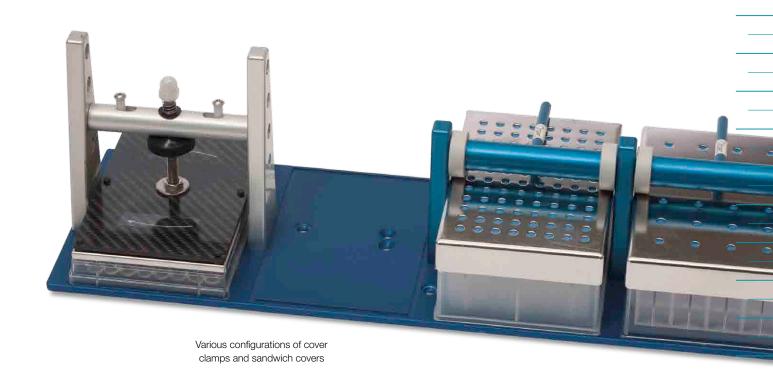
- Conversion of 24 and 96 microtiter plates (both deep- and low-well plates) into individual micro-reactors
- Low and uniform evaporation rates for every well
- Sterile barrier for individual wells prevents cross contamination
- Oxygen transfer rates similar to shake flasks in standard orbital shakers
- Simultaneous and reproducible sampling of 96 frozen glycerol stocks

- High throughput screening and distribution of mutant and construct libraries e.g. in E. coli or yeast
- Metabolic flux studies and high-throughput screening for high activity prokaryotic or eukaryotic mutants
- · Comparative studies, e.g. clinical isolates
- Growth medium optimization for cell lines or production strains



Cross-section of Micro-Flask sandwich cover

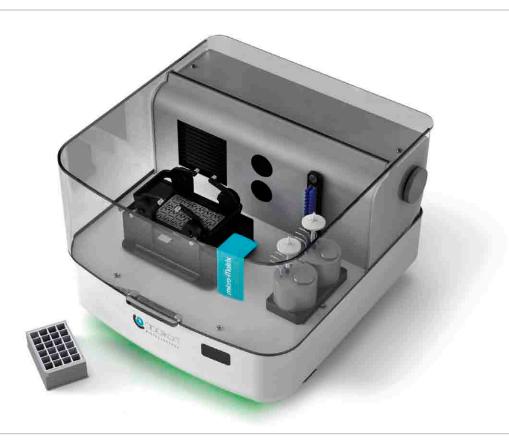
Type of microtiter plate	Well volume	Culture volume	Orbital shaking	Shaking amplitude	O ₂ -transfer rate (30°C, air, 1 bar)	Headspace refreshment	Evaporation rate per well (at 30°C)	at 30 ampl.	pattern 0 rpm ampl.
			frequency			rate	(at 30 C)	25 mm	50 mm
24-square deep-well polypropylene, 17x17 mm, depth 40 mm	11000 µl	2500 µl 2500 µl 2500 µl 4000 µl	300 rpm 300 rpm 220 rpm 300 rpm	50 mm 25 mm 50 mm	51 mmol O ₂ /I/h 39 mmol O ₂ /I/h 35 mmol O ₂ /I/h 24 mmol O ₂ /I/h	2.5 ml / min (1 VVM)	50% humidity: 50 µl H ₂ O per day 75% humidity: 25 µl H ₂ O per day		
		4000 µl	220 rpm	25 mm	24 mmol O ₂ / I / h	(0.6 VVM)	20 μι 11 ₂ 0 μει ααγ	2500 µl	2500 μ
24-round low-well polystyrene, Ø 16 mm, depth 18 mm	3000 µl	750 µl 750 µl 1000 µl 1000 µl	300 rpm 300 rpm 300 rpm 300 rpm	50 mm 25 mm 50 mm 25 mm	40 mmol O ₂ /I/h 25 mmol O ₂ /I/h 30 mmol O ₂ /I/h 19 mmol O ₂ /I/h	1.1 ml / min (1.4 VVM) 1.1 ml / min (1.1 VVM)	50% humidity: 30 µl H ₂ O per day 75% humidity: 15 µl H ₂ O per day	1000 µl	1000 µ
96-square deep-well polypropylene, 8x8 mm, depth 40 mm	2400 µl	500 µl 500 µl 750 µl 750 µl 1000 µl	300 rpm 300 rpm 300 rpm 300 rpm 300 rpm 300 rpm	50 mm 25 mm 50 mm 25 mm 50 mm 25 mm	38 mmol O ₂ /I/h 12 mmol O ₂ /I/h 24 mmol O ₂ /I/h 7 mmol O ₂ /I/h 18 mmol O ₂ /I/h 3 mmol O ₂ /I/h	1 ml / min (2 VVM) 1 ml / min (1.3 VVM) 1 ml / min (1 VVM)	50% humidity: 22 μl H ₂ O per day 75% humidity: 11 μl H ₂ O per day	750 µI	750 µl
96-round low-well polystyrene, Ø 6.5 mm, depth 11 mm	380 µl	100 µl 100 µl 150 µl 150 µl 200 µl 200 µl	300 rpm 300 rpm 300 rpm 300 rpm 220 rpm 300 rpm	50 mm 25 mm 50 mm 25 mm 50 mm 25 mm	39 mmol O ₂ /I/h 20 mmol O ₂ /I/h 32 mmol O ₂ /I/h 16 mmol O ₂ /I/h 12 mmol O ₂ /I/h	250 µl / min (2.5 VVM) 250 µl / min (1.7 VVM) 250 µl / min (1.3 VVM)	50% humidity: 6 μ l H ₂ O per day 75% humidity: 3 μ l H ₂ O per day	150 µl	150 µІ



micro-Matrix:

24 bioreactors in a convenient microtiter format

- Independently controlled bioreactors accelerate development
- Liquid feeding enables true scale-down studies
- Simple, powerful software streamlines operator workflow



Introduction

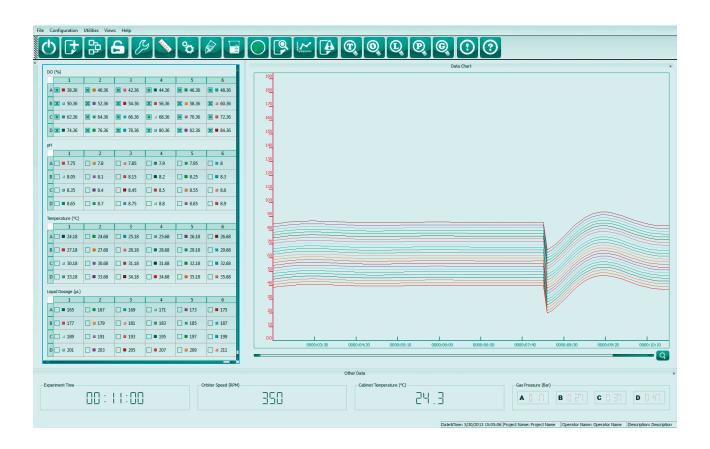
The unique micro-Matrix offers total control over 24 independent bioreactors in a simple microtiter plate footprint. Each of the 24 bioreactors on a plate offer independent controls like its larger stirred-tank relatives:

- pH (measurement and two-sided control)
- temperature (measurement and control, including plate-wide gradients)
- dissolved oxygen control (measurement and two-sided control)
- individual liquid additions (including feeding profiles)
- Up to 4 separate gas additions (individually controlled).

The micro-Matrix is a true scale down of small scale bioreactors. The bioreactor square well cassette design is based upon our popular SBS-format microtiter plates that maximize mixing, optimize gas transfer, and seamlessly integrate into lab automation protocols. The PC-based human interface of the micro-Matrix reflects our popular my-Control interface and offers simple, intuitive interaction with each of the 24 bioreactors. Integrated LEDs indicate the status of the bioreactors (inactive / active / alarm) with color-based feedback so that operators can get instant process information with one quick glance.

Software

The micro-Matrix software offers an easy way to operate 24 bioreactors in parallel, plus simple comparisons of large numbers of experimental cultures. Using an instinctive leftto-right progression, the interface guides operators through experimental setup, instrument configuration, control strategy definition, and data visualization. It is also possible to define time- and event-based control actions, and all data can be exported from the instrument mid-cultivation.

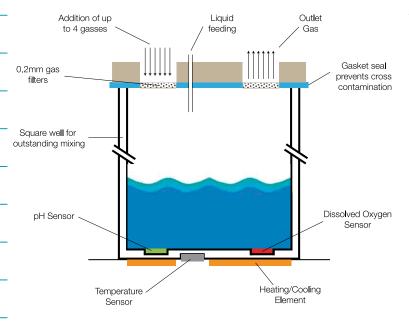


Measurement and control

Each bioreactor has its own PID controller for pH, dissolved oxygen, and temperature. Individual pH control can be achieved via gas addition, liquid addition, or a combination of both. Dissolved oxygen level can be individually controlled by up to four gas additions per bioreactor. Temperature can be individually controlled by the integrated cooling and heating system on a well-by-well basis, and users can define temperature gradients across the set of bioreactors.

Advanced control strategies are also available to users interested in cascade controls (up to 5 actuators per process variable), time-based setpoint changes, and event-triggered liquid feeds. Liquid feeding is also available using varying types of addition profiles.

- · Screening of cell-line, microbial, and/or yeast libraries
- Process development studies
- Process optimization studies
- · Small volume cultivations



Schematic diagram illustrating the functioning of the micro-Matrix control loops.

Technical data

Each of the four gas feeds and one liquid entry are controlled individually per bioreactor (5 additions per reactor).

- Independent gas supplies: for Air / O₂ / N₂ / CO_2 / NH_3
- Integrated liquid feed individually per well
- Cascade up to five actuators per control loop per
- Control strategy is user definable per bioreactor per experiment
- Temperature measurement and control per reactor
- pH measurement and control per reactor
- DO measurement and control per reactor
- Orbital shaker 0-350 rpm @ 25 mm orbit

Cassettes

The polystyrene bioreactor cassettes conform to the SBS standard for 24 well culture plates (128x86 mm). The total volume per bioreactor is 10 ml with working volumes from 1 to 7 ml (recommended working volume is 5 ml). The square bioreactors are designed based upon our popular 24-well microtiter plate design to optimize mixing and gas transfer, and Applikon has characterized these plates to offer advice on proper selection of working volume and agitation to achieve your process goals. Cassettes are delivered beta-sterilized and sealed in a light shielding package.



Connections

The micro-Matrix requires connection to a standard 230/115V AC power supply and pressurized gas and (air, oxygen, nitrogen, carbon dioxide). The micro-Matrix is connected to a computer through a standard Ethernet port.

Total volume per bioreactor well	10 ml	
Working volume per bioreactor well	1 - 5 ml	
Orbit radius	25 mm diameter	
RPM range	0 - 400 RPM	
Gas delivery	0.1 - 18 ml / min	Per gas, per well
Number of gasses	4	
Gas feed pressure	> 1.0 (extern)	
Liquid delivery	> 50 nl	
Liquid feed pressure	> 2.0 bar (extern)	
Temperature measurement range	0 - 45 °C	
Resolution	0.1 ℃	
Accuracy	0.5 ℃	
Temperature control range	15 - 45 ℃	
ΔT between adjacent wells	1℃	
Heat-up time	1 °C / min	20 °C to 37 °C
Control accuracy	± 0.1 °C	
pH measurement	5.5 - 8.5 pH	
Resolution	< 0.05 pH	@ pH 7.2
Accuracy	< 0.1 pH	@ pH 7.2
pH control range	5.5 - 8.5 pH	
Control accuracy	± 0.1 pH	
DO measurement	0 - 150 %	Air saturation
Resolution	< 1 %	Air saturation
Accuracy	< 0.5%	@ 0% air saturation
	< 3%	@ 100% air saturation
DO control range	0 - 150 %	
Control accuracy	± 5%	Air saturation
Dimensions	415 mm	Height
	570 mm	Depth
	560 mm	Width
Weight	65 kg	
Oxygen Transfer Rate	250 mmol / l / h	
Mixing times	< 1 sec	

Mini bioreactors, real small... real bioreactors

The MiniBio range of bioreactors (250 ml, 500 ml and 1000 ml total volume) is a true scale down of the laboratory scale bioreactor. The MiniBio systems have the same flexibility as the laboratory scale bioreactors. This means that the MiniBio systems can be customized to fit the demands of any process. The small volume reduces media costs and maximises bench space, which is normally at a premium.

Features

- Generate more data in less time
- Easy setup and operation
- Cultivate using less medium
- Cultivate using less bench space
- Generate scalable results

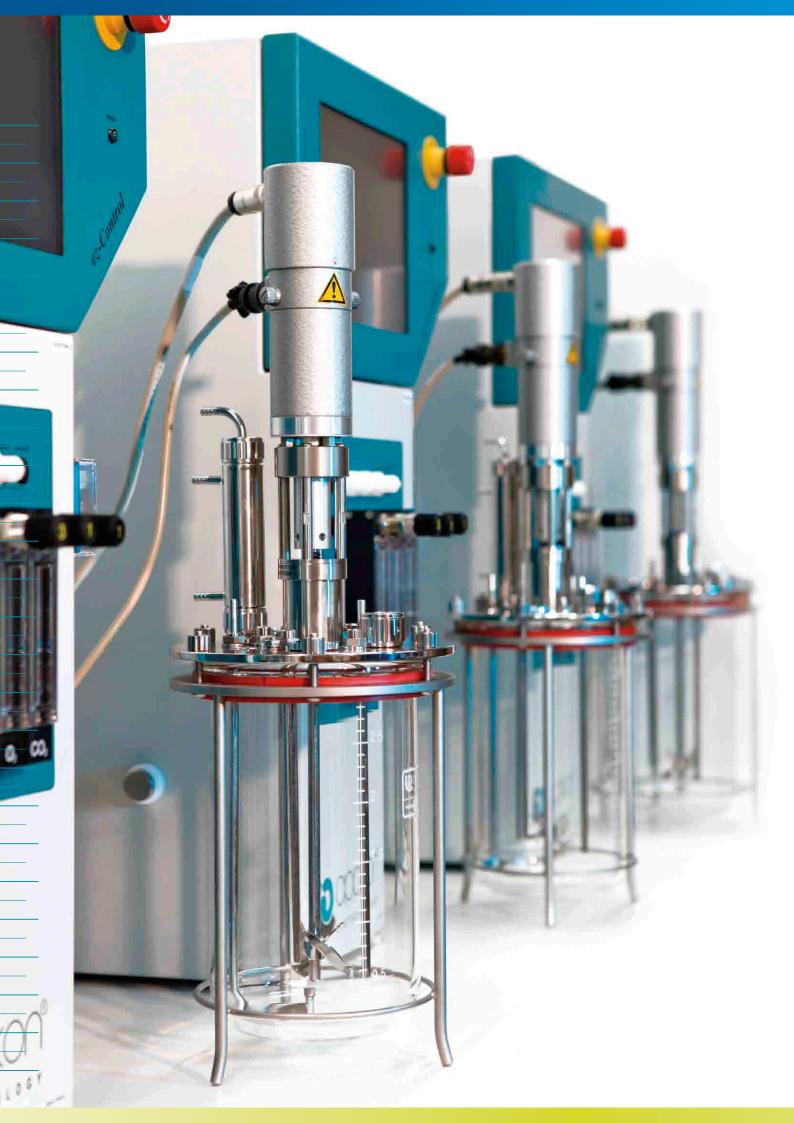
- Screening studies
- Media optimization
- Process optimization
- Microbial and Cell culture Batch, Fed-Batch, Perfusion and Continuous cultivation





Color your lab

	MiniBio 250	MiniBio 500	MiniBio 1000				
Total volume (ml)	290	550	1000				
Working volume (ml)	200	400	800				
Minimum working volume (ml)	50	100	200				
Aspect ratio total volume	2.3	2.1	2.3				
Aspect ratio working volume	1.6	1.5	1.9				
Dimensions (dxh)	180 x 400 mm	195 x 400 mm	200 x 550 mm				
Dimensions for autoclaving (dxh)	180 x 250 mm	195 x 250 mm	200 x 400 mm				
Orive system	Direct drive, lipsealed	Direct drive, lipsealed	Direct drive, lipsealed				
Maximum stirrer speed (rpm)	50 - 2000	50 - 1750	50 - 1500				
Maximum impeller tip speed (m/s)	2.3	2.0	3.5				
mpellers	Choice of Rushton and m	Choice of Rushton and marine					
Gas sparger	Porous sparger or L-type	Porous sparger or L-type sparger					
Gas overlay	Yes	Yes					
Exhaust gas	Electrically cooled exhaus	Electrically cooled exhaust gas condenser (evaporation <4% per day at 37°C @ 2vvm)					
Sampling	Fixed sample pipe with or	otional sampling system					
Draining	Height adjustable drain pi	ре					
Additions	4 fixed inlet ports and opt	ional micro liquid injectors					
Н	Measurement: 8 mm classic pH sensor						
	Control: via acid pump (va	ariable speed pump) or CO_2 g	as				
	in combination with alkali pump (variable speed pump)						
002	Measurement: 8 mm classic polarographic DO ₂ sensor						
	Control: via a combination	n of N_2 , Air, O_2 (optional MFC)					
	and agitation or nutrient a	ddition (variable speed pump)					
Temperature	Measurement: Pt-100 ser	nsor in thermowell in topplate					
	Control: electrical cooling	and heating jacket via bioread	ctor wall				
-oam	Measurement: Height adj	ustable conductivity based for	am sensor				
	Control: Anti foam additio	n (variable speed pump)					
_evel	Measurement: Height adj	ustable conductivity based lev	rel sensor				
	Control: variable speed p	ump for liquid addition or remo	oval				
Optional inlets	Septum, chemostat tube,	liquid entry system					
Optional sensors	Biomass, Optical Density,	O ₂ and CO ₂ off gas.					



Glass autoclavable bioreactors, the world wide standard

In the laboratory bioreactor and fermentor range Applikon is worldwide market leader because of its dependable and easy to use systems. The bioreactors and fermentors excel in quality and modularity. An Applikon laboratory system is easy to upgrade if a change in research activities occurs. Applikon offers glass autoclavable bioreactors for cell culture applications and glass autoclavable fermentors for microbial culture applications. The systems are built according to the specific demands of a process using an extensive array of standard components. Because of the modularity and flexibility, the user can always adapt the systems to changed process demands. This results in low initial investment and low running costs. The stirred tank reactor (STR) is the most widely used bioreactor type. Glass autoclavable bioreactors and fermentors are available in 1 - 2 - 3 - 5 - 7 - 15 and 20 liter total volume.

Features

- Wide range of volumes with interchangeable modules
- Wide range of modules to tailor the systems to the research demands
- No welded parts in the bioreactor topplate
- Simple set-up and easy to handle
- Optional high torque magnetically coupled agitator
- All metal parts are constructed of stainless steel 316L
- External mirror polished finish
- Electropolished finish of product contact stainless steel parts ease cleanability
- Glass dished bottom vessels are made of borosilicate glass to guarantee:
 - resistance to thermal shock
 - excellent corrosion resistance
 - smooth, non porous surface for easy cleaning
 - optimal transparency for visual inspection of the culture
- Glass bioreactor vessels can be used up to 0.5 barg (7.5 psig) of overpressure.

- Microbial cultures
- Cell cultures
- Batch
- Fed-Batch
- Perfusion
- · Continuous cultivation





	Total volume (L)	Working volume (L)	Minimum working volume (L)	Aspect ratio total volume (L)	Aspect ratio working volume (L)		
1 liter	1.25	0.9	0.3	2.1	1.5		
2 liter single wall	2.2	1.7	0.5	2.2	1.9		
2 liter jacketed	2.2	1.7	0.5	2.2	1.9		
3 liter single wall	3.1	2.7	0.5	1.9	1.5		
3 liter jacketed	3.1	2.7	0.5	1.9	1.5		
5 liter single wall	4.8	3.4	0.9	1.6	1.1		
5 liter jacketed	4.8	3.4	0.9	1.6	1.1		
7 liter single wall	6.8	5.4	1.5	2.2	1.8		
7 liter jacketed	6.8	5.4	1.5	2.2	1.8		
15 liter single wall	16.5	12	3.0	1.7	1.5		
15 liter jacketed	18.2	12	3.0	1.5	1.2		
20 liter single wall	23.4	16	3.0	2.4	2.0		
<u> </u>	Internal Dia	meter (mm)	Internal Height (mm)	Autoclave dir	nensions (WxH mn		
1 liter	95		200		72 x 393		
2 liter single wall	105	5	240	ø1	90 x 436		
2 liter jacketed	105	5	240	ø2	19 x 486		
3 liter single wall	130)	240	ø1	90 x 436		
3 liter jacketed	130)	240	ø2	35 x 436		
5 liter single wall	160)	250	ø2	60 x 436		
5 liter jacketed	160)	250	ø2	60 x 480		
7 liter single wall	160)	350	ø2	60 x 600		
7 liter jacketed	160)	350		64 x 645		
15 liter single wall	222)	440		81 x 710		
15 liter jacketed	240)	440		91 x 740		
20 liter single wall	222)	620		81 x 900		
Drive system	Direct drive, li	ipsealed or mag	netically coupled				
Maximum stirrer speed (rpm)	Standard range is 50 - 1250.						
	1, 2 and 3 lite	er systems can b	e supplied with 2000 rpm	n motor			
Impellers	Rushton and	marine with out	side diameters 45 mm, 60) mm 75 mm or 85	5 mm		
Gas sparger	Rushton and marine with outside diameters 45 mm, 60 mm 75 mm or 85 mm Porous sparger or L-type sparger						
Gas overlay	Yes						
Exhaust gas	Water cooled	exhaust gas co	ndenser				
Sampling	Fixed height of	or height adjusta	ble sample pipe with opti	onal sampling syst	:em		
	Sample pipe	internal diamete	rs choices are: 1.7 mm, 4	mm, 6 mm or 10	mm		
Draining	Drain pipe						
Additions	Triple or single	e inlet ports and	optional micro liquid injec	etors			
pH	Measurement	t: 12 mm classic	pH sensor				
	Control: via a	cid pump or CO	2 gas (rotameter or MFC)	in combination wit	th alkali pump		
DO ₂	Measurement	t: 12 mm classic	polarographic DO ₂ sens	or			
	Control: via a	combination of	N ₂ , Air, O ₂ (Rotameter or	MFC) and agitatio	n or		
	nutrient addit						
Temperature	Measurement	t: Pt-100 sensor	in thermowell in topplate				
	Control: cooli	ng and/or heatir	ng jacket via bioreactor wa	all or via internal he	eat exchanger		
Foam			ble conductivity based fo		-		
		foam addition p	-				
Level			ble conductivity based le	vel sensor			
		p for liquid addit	-				
Optional inlets			uid entry system				

Photo bioreactors, the next best thing to sunlight

a photobioreactor with no downtime and minimal investment.

The Applikon "PhotoBio" photobioreactor range is based on the standard Applikon re-usable and single-use bioreactors. Special light panels are added to these systems to allow the growth of photosynthesizing organisms (plants, algae, bacteria). The well proven design of the bioreactors in combination with the state-of-the-art LED light panels guarantee the best performance of the PhotoBio for any application. The light panels can be retrofitted to the Applikon bioreactors to turn your standard bioreactor into

Features

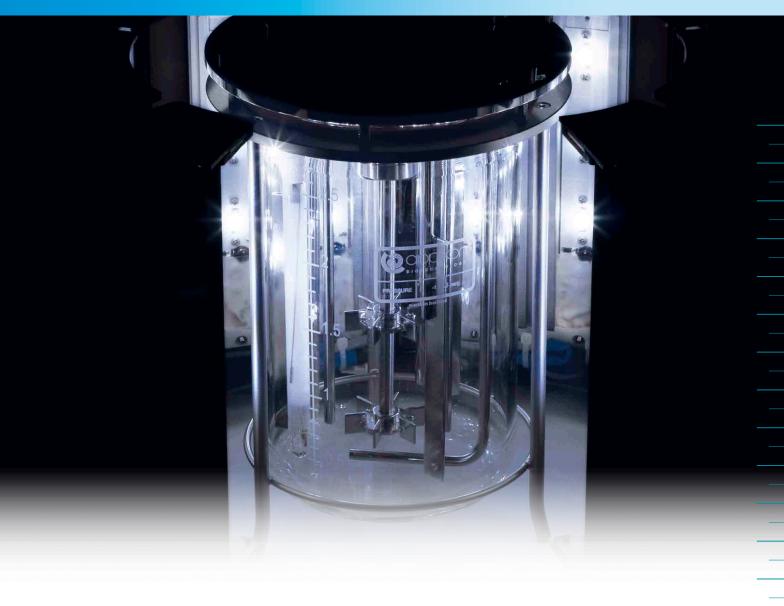
- Proven bioreactor design
- Long lifetime (100.000 hrs) in combination with good lumen maintenance
- Low voltage operation having more than 90% efficiency with no EMI radiation.
- Directional light output & even distribution of light over the target application area
- Great performance in cold environments
- · No heat generation

- Photo-synthetically Active Radiation (PAR) 400-700 nm, ideal for plant growth, to achieve better efficiency in the response of plants
- Excellent wavelength stability over time, consistent, high-reliability
- Usable wavelength blue (470 nm) and red (660 nm) for plant growth
- Fully regulated form 0 to 100% light intensities (0 to 20.000 lux) in real time

Applications

• The PhotoBio can be used for all photosynthesizing organisms (plants, algae, bacteria).





PhotoBioSU50

Maximum driving capacity	140 watt of power or 24 light bank of 6 watt
Programmable zones	8
Intensity control	0 to 100% PWM
Time base	Built in Real time clock
Time range	99:59 hours: minutes per step (maximum 9 time/intensity steps in one cycle)
Light driving	Constant current source
Housing & Protection Class	IP-30 and IP-65 for Control Panel and IP67 for Light bank
User interface	16 x 2 Backlit LCD, Feather touch keys
Serial Communication port	Full duplex RS232 or RS485 interface(optional)
Ambient temperature	0 °C up to 60 °C
Power supply	115 / 230 V AC, 50-60 Hz
Power consumption	Maximum 150 W

The PhotoBio range of bior	reactors consist of the following products:	
PhotoBioSTR2	2 liter stirred tank bioreactors (single wall, non jacketed),	40 Watt panel
PhotoBioSTR3	3 liter stirred tank bioreactors (single wall, non jacketed)	40 Watt panel
PhotoBioSTR5	5 liter stirred tank bioreactors (single wall, non jacketed)	60 Watt panel
PhotoBioSTR7	7 liter stirred tank bioreactors (single wall, non jacketed)	60 Watt panel
PhotoBioSTR15	15 liter stirred tank bioreactors (single wall, non jacketed)	120 Watt panel
PhotoBioSTR20	20 liter stirred tank bioreactors (single wall, non jacketed)	120 Watt panel
PhotoBioSU10	10 liter single use AppliFlex rocking bioreactors	40 Watt panel
PhotoBioSU20	20 liter single use AppliFlex rocking bioreactors	60 Watt panel

120 Watt panel

50 liter single use AppliFlex rocking bioreactors

Single use bioreactors

Applikon offers several types of single-use bioreactors: AppliFlex, rocking bioreactors from 10 to 50 liter, HyPerforma SUB stirred tank bioreactors in the range of 66 to 2,700 liter total volume, PALL PAD square bioreactors in the range of 25 to 2,500 liter total volume and

PALL iCellis Nano bioreactors for cultivating anchorage dependable cells. All systems are unique in their accurate measurement and control of key process parameters.

The systems can be controlled using the Applikon ez-Control, i-Control or my-Control. Most systems can be equipped with re-usable sensors as well as fluorophor pH and Dissolved Oxygen sensors. All systems are supplied turnkey and fully documented. All systems go through standard IQ/OQ and FAT procedures before they are delivered and installed at the customers site. The qualified Applikon technical support team can take care of the installation and will be your first point of contact for any questions. Our delivery includes the bioreactor, the controller, sensors, actuators, temperature control system, supervisory software and validation documentation. Our well trained sales consultants are able to advise you on the complete configuration of your single use bioreactor system.



AppliFlex

The AppliFlex bioreactor range consists of a 10 liter, 20 liter and 50 liter bioreactor bag. The control system (pH, Dissolved Oxygen, temperature, mixing) is the standard Applikon ez-Control. The rocking motion offers gentle mixing. The same rocker can be used for the 10 (2x), 20 and 50 Liter bioreactor bags. The AppliFlex bioreactors are an easy scale-up to the HyPerforma bioreactors; the bags are made of the same materials which eases validation.



HyPerforma® S.U.B.

The HyPerforma® S.U.B. provides all the advantages of single-use bioprocessing in a classical stirred tank bioreactor system design. The critical design parameters of the S.U.B., such as height to diameter ratios, mixer design and location and typical control system interfaces, have been maintained. The S.U.B. is available with new optimized standard BioProcess Containers with improved dual sparge capability. Open pipe and frit sparging systems are included to provide a wider range of operating conditions. A key element to the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linked to an external mixer drive. The range includes units with maximum working volumes of 50, 100, 250, 500, 1,000 and 2,000 L.

PALL iCELLis™ Nano

The PALL iCELLis™ Nano system, is designed to simplify your process by combining the advantages of single-use technologies with the benefits of a fixed-bed system. Central to the iCELLis bioreactor technology is the use of a compact fixed-bed, filled with macrocarriers. This matrix is made of medical grade polyester microfibers and provides up to 4 m² available area for cell growth in only 200 ml volume.

This is the surface-equivalent of 47 roller bottles. The iCELLis bioreactor is provided with pre-packed macrocarriers. Evenlydistributed media circulation is achieved by a built-in magnetic drive impeller, ensuring low shear stress and high cell viability. The cell culture medium flows through the fixed-bed from the bottom to the top. At the top, the medium falls down the outer wall as a thin film where it takes up O_2 to maintain high k_L a the in the bioreactor.

• iCELLis nano Fixed-bed height 10 cm

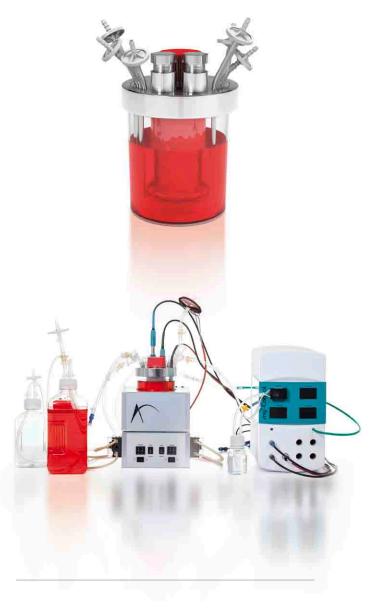
 Fixed-Bed Volume 0.2 L

• Culture Surface Area 4 m²

• Equivalent CS10 (6,300 cm²) 6

• Equivalent RB (850 cm²) 47





PALL PadReactor

The PALL PadReactor system is perfectly suited to laboratory environments, process development centers, clinical material supply and flexible GMP manufacturing. The square bioreactor vessel, which offers comparable functionality to classical stirred tank bioreactors, is a single-use bag integrating an internal paddle mixing and sparger system. The sparger is integrated in the paddle mixer to enhance oxygen transfer rates. The innovative bag design improves mixing at low shear forces and allows a non-invasive stirrer connection to the system. The paddle is enclosed in a medical grade ULDPE sleeve, made from the same contact material as the bag itself, and is coupled on top of the vessel with the mechanical mixing head. The PadReactor is available in total volumes of 25L, 50L, 250L, 600L, 1200L and has been used successfully in cultivation of anchorage dependent and suspension cells.

1	AppliFlex	10	25	50				
	Total volume (L)	10	25	50				
	Max working volume (L)	5	12.5	25				
(()	Min working volume (L)	2	5	10				
-	HyPerforma	50	100	250	500	1000	2000	
	Total volume (L)	66	120	316	660	1320	2700	
	Max working volume (L)	50	100	250	500	1000	2000	
	Min working volume (L)	25	50	125	250	500	1000	
24	Pad	Mini	25	50	125	250	600	1200
	Total volume (L)	16	25	50	125	250	600	1200
	Max working volume (L)	13	20	40	100	200	480	960
IF X	Min working volume (L)	3.2	8	10	25	25	120	240
Dark See and	iCellis Nano							
THE	Volume (L)	0.04	0.08	0.2				
	Surface area Low (m ²)	0.53	1.06	2.6				
	Surface area High (m²)	0.8	1.6	4				

Sensors	Fluorophor pH	Fluorophor Dissolved Oxygen	Gel filled sterilizable pH	Sterilizable Polarographic Dissolved Oxyg	Temperature en
Measuring range	5.5 8.5 pH	0 100%	0 12 pH	0 100%	0 150°C
		O_2 saturation		O ₂ saturation	
Accuracy	± 0.1 pH	± 0.4%	± 0.1 pH	± 2%	0.1°C
Measuring temperature range	0 - 40°C	0 - 40°C	0 - 80°C	0 - 60°C	0 150°C
Maximum temperature	45°C	45°C	135°C	135°C	150°C
Sensor life time	2 weeks @	6 months	> 1 year	> 1 year	> 1 year
	1 measurement				
	per minute				
	3.5 weeks @				
	1 measurement				
	per 2 minutes				

Features & Applications

- Simple operation
- OPC compliant controller
- Accurate process control
- Classic and single-use (fluorophor) sensors for measurement of pH, Dissolved Oxygen
- Accurate control of pH, DO, temperature, mixing
- Data logging & SCADA (21CFR part 11) available
- Turn-key delivery
- IQ/OQ/FAT and SAT for the complete system

- Fully documented delivery eases validation
- One point of contact for the complete system
- Qualified support and service
- Cell culture
- Batch
- Fed Batch
- Perfusion
- Suspension cells
- Anchorage dependent cells

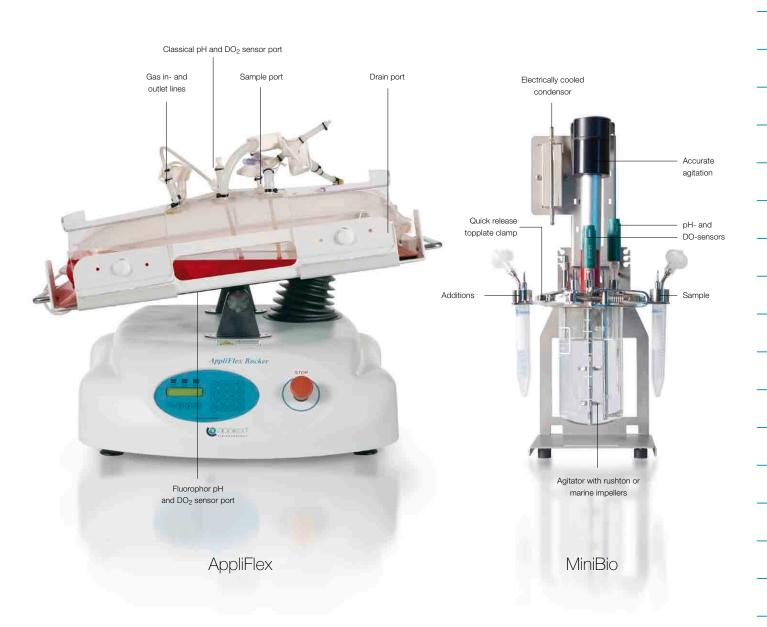
BioBundle, complete cultivation systems

A BioBundle is a complete bioreactor system, equipped with all necessary components and is ready to use "out-of-the-box". No detail is overlooked: the system is complete with silicone tubing, sample bottles and a "starter kit" including spare parts. The BioBundle is easy to set-up, requires no special skills or tools, easy to learn and easy to operate. BioXpert Lite Software for data acquisition is included. Select one or more of the optional add-on packs to customize your BioBundle. The BioBundle provides a unique



combination of ease of use and sophistication, reducing the time to start-up a process. The system is equipped with the intelligent and powerful process controller: easy and intuitive to operate, such that the user manual might not be needed.

The process controller has control loops for pH, Temperature, Dissolved Oxygen, Foam/Level and agitation and can apply a combination of digital and analog outputs for process control. Actuators such as rotameters, solenoid valves, mass flow controllers, pumps, thermocirculator and others can be controlled. The operator can set P-I-D values, dead-band for pH control, cascade control strategies, and dose monitors for liquid additions. The advanced auto-tuning adaptive control system is part of every bundle and takes the guessing out of PID controller setting. The system can automatically and continuously calculate the best controller settings for every process.



Modularity and configurability

Although the BioBundle has a pre-set configuration, the whole bioreactor system remains modular and configurable. With simple changes in configuration the BioBundle system can be modified for different applications in a cost-effective way! This applies to changes in process control strategies, in using extra gas or liquids, but also in changing the system into a microbial or cell culture set-up.

Compact design

The BioBundle is designed to occupy as small a footprint as possible. All accessories such as pumps and gas flow control valves are conveniently integrated in a compact console. The compact design reduces the need for expensive lab space.

Software for data acquisition and supervisory control

The BioBundle control system includes an Ethernet connection port to connect to a PC with software for data acquisition or SCADA such as the Applikon BioXpert packages.

BioXpert Lite (data acquisition) is included in this BioBundle. Multiple bioreactors can be connected to one PC for data acquisition.

Optional BioXpert packages are BioXpert 2 and BioXpert W7: SCADA of multiple bioreactors, including cGMP production applications.

Cost Saving

The BioBundle is a pre-packed system. The assembling of the BioBundles in series provides a cost saving which is for the benefit of the customer.

Summarising

Over all some of the benefits Applikon bioreactors provide include:

- dependable and reliable operation = greater productivity and yield
- modular design = less cost in the future
 - (being able to use same equipment for different applications)
- less downtime due to maintenance = greater economy in operation, higher yield to cost ratio
- simple operation = less operator training required

	MiniBioBundle	MiniBioBundle	BioBundle	BioBundle	AppliFlex
	Cell Culture	Microbial	Cell Culture	Microbial	BioBundle
Control system	my-Control	my-Control	ez-Control	ez-Control	ez-Control
Total Volume	250ml, 500 ml,	250ml, 500 ml,	1L, 2L, 3L, 5L,	1L, 2L, 3L, 5L,	10L, 20L, 50L
	1000ml	1000ml	7L, 15L, 20L	7L, 15L, 20L	
Working Volume	200ml, 400ml,	200ml, 400ml,	0.9L, 1.7L, 2.7L,	0.9L, 1.7L, 2.7L,	5L, 10L, 25L
	800ml	800ml	3.2L, 5.4L, 12L, 16L	3.2L, 5.4L, 12L, 16L	
Agitator	Lipseal with	Lipseal with	Lipseal with	Lipseal with	Mixing by
	marine impeller	Rushton impellers	marine impeller	Rushton impellers	rocking motion
Aeration	Air supply via	Air supply via	Air and Oxygen	Air and Oxygen	Air and Oxygen
	sparger	sparger	supply via sparger	supply via sparger	supply via overlay
				and overlay	
Exhaust gas	Optional gas outlet	Gas outlet	Gas outlet	Gas outlet	
	condenser	condenser	condenser	condenser	
Sampling	Sample pipe	Sample pipe	Sample pipe	Sample pipe	Sample line
	included	included	included	included	included
	Sample system	Sample system	Sample system	Sample system	Sample system
	optional	optional	optional	optional	optional
pH	Measurement via	Measurement via	Measurement via	Measurement via	Measurement via
	pH sensor control	pH sensor control	pH sensor control	pH sensor control	pH sensor control
	via liquid alkali	via liquid alkali or	via liquid alkali	via liquid alkali and	via liquid alkali
	pump and CO ₂	acid addition pump	pump and CO ₂	acid addition pump	pump and CO ₂
	gas supply		gas supply		gas supply
Temperature	Measurement via	Measurement via	Measurement via	Measurement via	Measurement via
	Pt-100	Pt-100	Pt-100	Pt-100	Pt-100
	Heating only via	Heating and	Heating only via	Heating via heating	Heating only via
	heating blanket	cooling via	heating blanket	blanket cooling by	heating blanket
		Peltier system		cold water in heat	
				exchanger	
Dissolved Oxygen	Measurement via	Measurement via	Measurement via	Measurement via	Measurement via
	DO ₂ sensor control	DO ₂ sensor control	DO ₂ sensor control	DO ₂ sensor control	DO ₂ sensor contro
	via Air and O ₂ gas	via Air supply and	via Air and O ₂ gas	via Air and O ₂	via Air and O ₂ gas
	supply	agitation speed	supply	supply and agitation	supply
				speed	
Foam	Option	Measurement via	Option	Measurement via	
		Measurerrierit via			
		Foam sensor	·	Foam sensor	
		Foam sensor			
				Foam sensor	
	Option	Foam sensor control via anti-foam		Foam sensor control via anti-foam	
Level	Option 4 fixed in topplate	Foam sensor control via anti-foam addition pump		Foam sensor control via anti-foam addition pump	One inoculum and
Level Liquid additions	·	Foam sensor control via anti-foam addition pump Option	Option	Foam sensor control via anti-foam addition pump Option	One inoculum and alkali inlet.
Level	4 fixed in topplate	Foam sensor control via anti-foam addition pump Option 4 fixed in topplate	Option 3 ports in triple	Foam sensor control via anti-foam addition pump Option 3 ports in triple inlet,	
Level	4 fixed in topplate and 1 septum port	Foam sensor control via anti-foam addition pump Option 4 fixed in topplate and 1 septum port	Option 3 ports in triple inlet and one inoculum port.	Foam sensor control via anti-foam addition pump Option 3 ports in triple inlet, one inoculum port 1 and septum port.	alkali inlet.
Level	4 fixed in topplate and 1 septum port One liquid storage	Foam sensor control via anti-foam addition pump Option 4 fixed in topplate and 1 septum port Two liquid storage	Option 3 ports in triple inlet and one inoculum port. One liquid storage	Foam sensor control via anti-foam addition pump Option 3 ports in triple inlet, one inoculum port 1 and septum port. Three liquid storage	alkali inlet. One liquid storage
Level	4 fixed in topplate and 1 septum port	Foam sensor control via anti-foam addition pump Option 4 fixed in topplate and 1 septum port	Option 3 ports in triple inlet and one inoculum port.	Foam sensor control via anti-foam addition pump Option 3 ports in triple inlet, one inoculum port 1 and septum port.	alkali inlet.

my-Control is our most advanced bioreactor controller for small scale bioreactors starting at 50 ml (working volume). The system can control bioreactors up to a total volume of 3 L. This versatile controller can be used for both cell culture and microbial cultures. The advanced software makes it possible to switch from microbial to cell culture configuration in seconds. With its footprint of only 19 by 35 cm (W x D) it uses the minimal amount of bench space, allowing to set up as many as 5 on 1 m width of bench space. The built-in web server allows the my-Control to be operated by any computer with a web browser (Internet Explorer, Mozilla Firefox, Apple Safari or Google Chrome). Wireless devices like iPad, iPhone or Android tablets or phones can also be used to operate

my-Control. The selectable colored band on the unit allows the system to be personalized

Features

and to fit your laboratory.

- Control of all bioprocess parameters (including pH, temperature, dissolved oxygen, agitation, foam and level)
- Selectable autotuning adaptive PID control for accurate control when process conditions change during the culture.
- Easy operation through web browsers (Windows PC, Apple PC, Linux PC, iPhone, iPad, Android tablet, Android phone)
- Parallel processing is enhanced by allowing up to 32 my-Controllers in one human interface
- Extended liquid additions options tuned to small scale cultivation via up to 6 digital variable speed pumps or micro addition valves for extremely accurate nanoliter volumes
- Enhanced gas addition strategies via 3 mass flow controllers
- No water connections needed due to electrical cooling and heating system for bioreactor and condenser
- Expandable control system with optional extra inputs and outputs
- USB connection for optional balances, Biomass or Fluorophor pH and DO sensors

- Ideal for screening, media optimisation, modelling, toxicity studies etc.
- Mini bioreactors
- Autoclavable bioreactors up to 3 liter volume
- Single Use Bioreactors up to 3 liter volume
- Microbial and Cell cultivation
- Batch, Fed-Batch, Perfusion and Continuous cultivation

Inputs	pH, temperature, dissolved oxygen, agitation, foam and level
	Optional: biomass and fluorophor pH and fluorophor dissolved oxygen
	Optional inputs 4 x analog in (0 - 10 V)
Control type	PID control with selectable autotuning adaptive control
Actuators	Up to 6 digital variable speed pumps or micro addition valves for addition
	of extremely accurate nanoliter volumes
	Up to 3 Mass Flow Controllers or 4 solenoid valves for gas flow control
	Electrical bioreactor heating via Peltier element or Heating Blanket
	Electrical bioreactor cooling via Peltier element
	Electrical condenser cooling via Peltier element
	Spare I/O: 8 x digital output, 4 x analog out (0/4 - 20 mA)
Additional features	Emergency stop connection, central alarm output,
	System status indication (inactive/active/alarm) by integrated colored light
Power	Pmax = 480 VA, 115 / 230 Vac
Dimensions (d x w x h)	350 x 190 x 400 mm (D x W x H)
	8.5 kg



in-Control, simply powerful

in-Control is a process controller for laboratory scale bioreactors. The system is a drop-in-replacement for our older ADI 1010 Bio Controller and ADI 1030 Bio Controller. The in-Control offers high level control on a small footprint. When you are running your bioreactors controlled by our ADI 1010 or ADI 1030 Bio Controllers, the in-Control can be used to increase the capabilities of your bioreactor system with a minimal investment and no downtime for your process. The controller can be used for both cell culture and microbial cultures. The intuitive human interface is a built-in color touch screen.

Features

- Control of all bioprocess parameters (including pH, temperature, dissolved oxygen, agitation, foam and level)
- Selectable autotuning adaptive PID control for accurate control when process conditions change during the culture.
- Easy operation through touch screen interface and through web browsers (Windows PC, Apple PC, Linux PC, iPhone, iPad, Android tablet, Android phone)
- Enhanced gas addition strategies via up to 4 Mass Flow Controllers
- Expandable control system with optional extra inputs and outputs
- USB connection for optional biomass or fluorophor pH and DO sensors and balances
- Ethernet communication to SCADA

- Replacement of ADI 1010 Bio Controller and ADI 1030 Bio Controller
- Autoclavable bioreactors up to 20 liter volume
- Single Use Bioreactors
- Microbial and Cell cultivation
- Batch, Fed-Batch, Perfusion and Continuous cultivation



Inputs	pH, temperature, dissolved oxygen, agitation, foam and level	
	Optional: biomass and fluorophor pH and fluorophor dissolved oxygen	
	Optional inputs 4 x analog in (0 – 10 V)	
Control type	PID control with selectable autotuning adaptive control	
Actuators	8 x digital outputs for heating, cooling, fixed speed pump, solenoid valves etc.	
	Up to 4 Mass Flow Controllers or 4 solenoid valves for gas flow control	
	Spare I/O: 4 x analog out (0/4 – 20 mA)	
Additional features	Emergency stop connection, central alarm output,	
Power	Pmax: 480 VA 230 / 115 Vac	
Dimensions (dxwxh)	322 x 312 x 210 mm	
Weight (kg)	7.2 kg	



ez-Control, total control at your fingertips

The ez-Control accurately controls pH, Temperature, Dissolved Oxygen, Foam/Level and Agitation in bioreactors and fermentors. The color touch screen interface guides the user through the intuitive operation. The adaptive control features allow the user to focus on the process while the controller keeps tight control on the important process parameters. What makes this controller unique are its ease of use, its small footprint, its flexibility and its accurate control. The optional ADDA board offers an additional 8 analog inputs, 4 analog outputs, 8 digital inputs and 8 digital outputs.

Features

- Simple operation
- Adaptive PID control
- OPC compliance
- User definable controlloop configuration
- Store, copy and reload process configurations
- Local data storage and display up to 72 hours
- Synoptic, trending and bar graph displays
- Multiple user levels

- Autoclavable bioreactors
- Steam in Place bioreactors
- Single Use Bioreactors
- Microbial and Cell cultivation
- Batch, Fed-Batch, Perfusion and Continuous cultivation





	Measurement range	Measurement accuracy	
рН	0 - 14 pH	0.01 pH	
Temperature	0 - 150 °C	0.1°C	
Dissolved Oxygen	0 - 100% saturation	0.1%	
Foam/Level	Conductivity based measurement	On / off control	
Agitation	0 - 1250 rpm	1 rpm	
	0 - 2000 rpm	1 rpm	
Analog in	8 x		
Analog out	4 x		
Digital in	8 x		
Digital out	8 x		
Fluorophor pH	Optional 5.5 - 8.5 pH	± 0.1 pH	
Fluorophor Dissolved Oxygen	Optional 0 - 100% saturation	± 0.1 %	
Biomass	Optional		
Display	10.4 Inch color display with resistive touchscreen		
Communication interfaces	1 x Ethernet port (computer communication)		
	2 x USB slave,		
	1 x USB master		
Control type	PID control with selectable auto-tuning adaptive control		
Actuators	Up to 3 fixed speed pumps		
	Up to 4 Mass Flow Controllers		
	Heating and cooling via thermocirculator, heating blanket, cooling water valve		
	Water cooled condenser connection		
Additional features	Emergency stop connection, central alarm output,		
	Color touch screen operation		
Process connections	2 x Gas outlet, water for condenser (in and out),		
	Water for temperature control (in and out)		
Power	230 Vac 50 Hb / 115 Vac 60 Hb		
Dimensions (dxwxh)	474 x 408 x 711 mm		
Weight (kg)	30 kg		

i-Control, the scalable control system

i-Control is an easy to operate bioreactor control system and utility console.

This scalable control solution is used to control processes in bioreactor systems from laboratory scale to pilot plant and production scale saving time and money during scale-up. The i-Control is available in a Single, a Dual bioreactor set-up as well as in a Quad (4 bioreactors) configuration. This standard control solution can be supplied with Allen Bradley or Siemens PLC's. Basic functionality includes advanced process control for numerous parameters, fully automatic sterilization and Clean In Place routines. The off-the shelf system is supplied pre-configured and ready to use.

Features

- Off-the shelf standard Solution
- Reliable control platform (Allen Bradley and Siemens hard- and software)
- Supplier independent solution based on industry standard hardware
- Local Control and local display
- Integrates with any factory automation system
- Cost effective
- Fully documented supply eases validation
- Can be used in a 21CFR part 11 compliant system

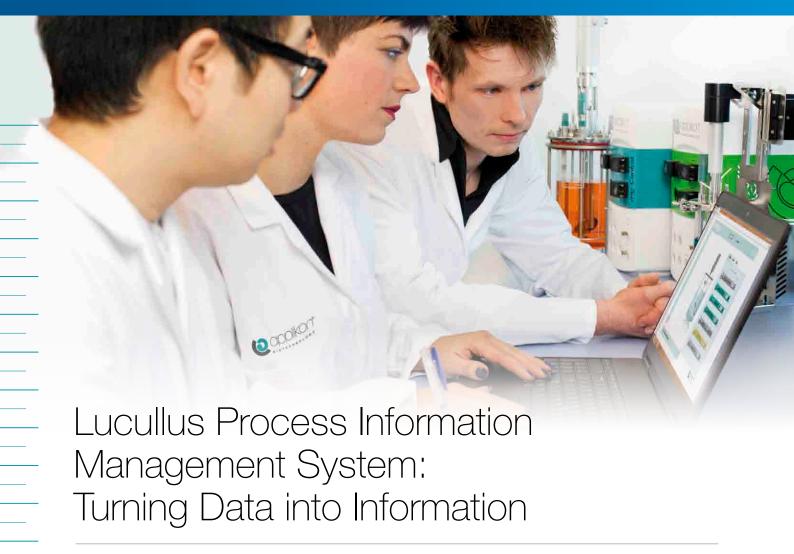
- Laboratory scale bioreactors
- Pilot plant scale bioreactors
- Production scale bioreactors
- Microbial cultures
- Cell cultures



pH/Temp input		
pH amplifier	Range	0 pH 14 pH
	Accuracy	± 0.01 pH
Temperature amplifier	Type	Pt 100 (3-wire type)
	Range	0°C +150°C
	Accuracy	± 0.1°C
DO/Level input		
DO amplifier	Type	Polarographic
	Range	0 % 500 % (air)
	Accuracy	± 0.1 %
Level amplifier	Type	On/Off signal
	Sensitivity	Software-selectable:
	High	Conductivity ≥ 26 μS equals "Contact"
	Low	Conductivity ≥ 200 µS equals "Contact"
2 Channel analog inputs	Range	4 – 20 mA
	Accuracy	± 0.1% Full Scale value
2 Channel analog outputs	Range	4 – 20 mA
	Accuracy	± 0.1% Full Scale value
2 Channel analog inputs for RTDs	Sensor Type	Pt-100
	Range	-200°C+800°C
	Accuracy	± 0.2 % Full Scale value
	Resolution	0.1°C







Lucullus Process Information Management System offers a new dimension in upstream bioprocess data management. Where classic SCADA solutions are limited to data acquisition and supervisory control functions, Lucullus integrates functionalities activities around the planning of recipes, reactor allocation, Design of Experiments, media preparation, media component trace-ability, data analysis, data mining, automatic reporting and modelling. The integration of all these functions into one comprehensive software solution saves the scientists time since all data is stored in one central Oracle[©] database. No more need for data export and import between different solutions, Lucullus integrates all functions needed for complete data management of your upstream process.

The ever increasing amount of process data generated by more sensors in smaller parallel bioreactor systems needs advanced software to turn this data into useful information. Lucullus PIMS offers a new dimension in data processing. Data management and data analysis is key for the future of R&D and process development in pharmaceutical industry. Lucullus PIMS software allows the user to monitor and control bioprocesses and offers an extensive toolbox for analyzing process data cross platforms. Process information can be generated based on data generated in different brands of bioreactor types and wide range of different cultivation volumes. The combination of the software with the broad range of Applikon Bioreactor Systems offer the user a unique system for validatable fast track development and basic research.

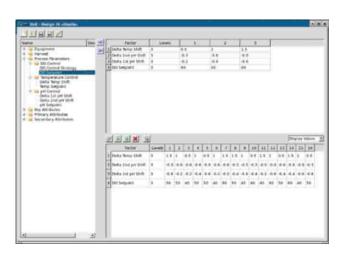
The main modules of Lucullus PIMS are

- Planning: activities around the planning of recipes, reactor allocation and Design of Experiments
- Preparation: media preparation, storage and component trace-ability
- Execution: process execution, data presentation, alarming and storage
- Evaluation: data analysis, presentation, automatic reporting, modelling and comparison of data between different cultures

Planning

Activities around the planning of recipes, reactor allocation and Design of Experiments

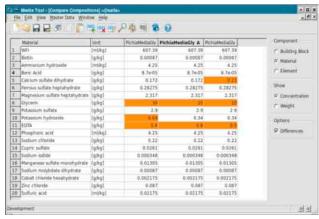
This module enables the user the optimum use of shared resources. The DoE module optimizes the experimental setup and guides the scientist through the optimal planning of experiments by selecting the different process parameters to be used in usually parallel experiments. The final result is doing more experiments with less resources due to optimal planning and coordination which leads to faster results in shorter time.



Preparation

Media preparation, storage and component trace-ability

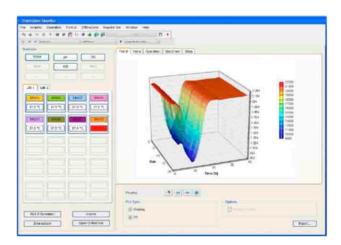
This module guides the user through the media preparation, media storage and planning of the use of the available media. Another part of this module keeps track of the batch of the raw components used in the media to allow full trace-ability of materials during the process. The process results can later on be compared by raw materials used or batches of media being used in different experiments. The ultimate goal of this module is the optimal use of materials in media preparation and preventing wrong conclusions based on experimental results where media components or batches might have played an important role.

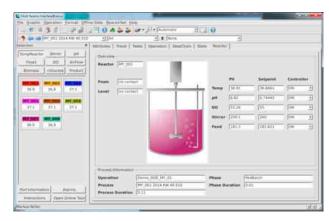


Execution

Data presentation, alarming and storage

The execution module is the heart of the program and is the part that is present in most SCADA systems. The execution module allows the scientist to define and execute the recipe for the process and present the process data in an optimal format. Data reduction techniques can be used to limit the amount of data stored in the Oracle database. Process data is stored per process and per process phase allowing simple comparison of the growth or production data of different experiments. Time and event based actions can be based on current process data from all active processes or on older experimental data allowing the system to predict what will be happening and to take preventive measures.

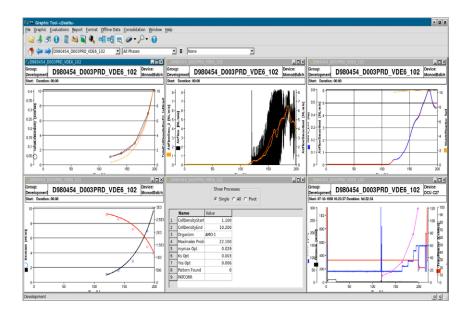




Evaluation

Data analysis, presentation, automatic reporting, modelling and comparison of data between different cultures

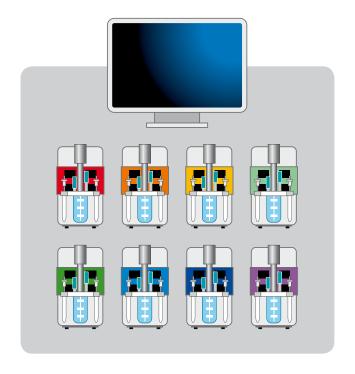
Evaluation is the part that will turn your data into valuable information. Scientist are gathering more and more data from processes, but without the right data processing, these data are useless. The Evaluation module of Lucullus PIMS is focused on turning process data across different platforms into comparable information and can help interpreting these data. One the many features is a pattern recognition function that allows the scientist to select a specific measurement pattern and search the database for comparable patterns. Only this feature can save days or weeks of work by one simple mouse click. Another important function is the automatic generation of batch reports. This will supply standardized batch reports independent of the operator or the cultivation hardware that has been used. Standardized reporting eases data interpretation and saves the scientist valuable time.



Lucullus PIMS can be supplied in three different architectures

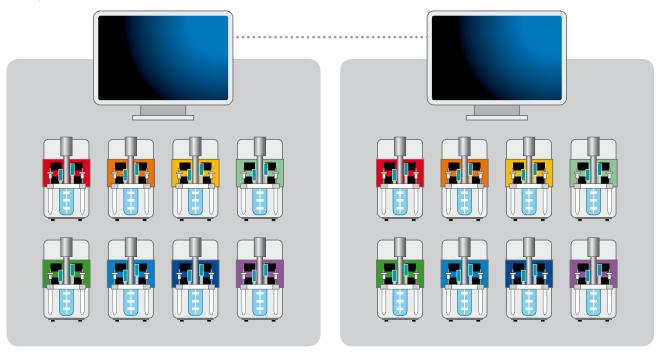
Stand alone edition

The stand-alone edition is used for up to 8 different bioreactors or one multi-bioreactor system on one computer. Data is stored in a local Oracle database and access to the process data can be through the local computer or via a remote network link to this process computer. Interactions to the process can be done through the local computer in the laboratory. It is advised to use a data safety system on the local computer to make sure your valuable process data are secured in case of computer hardware failures.



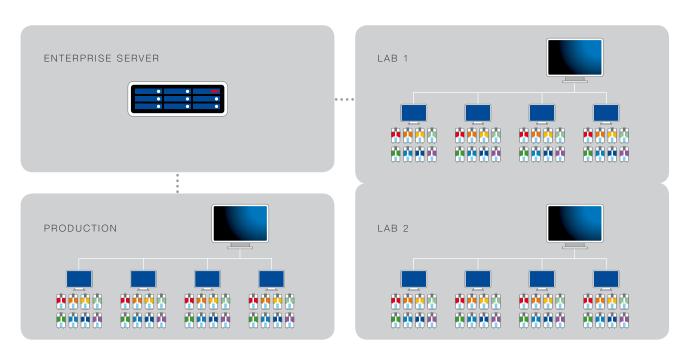
2 | Client Server Edition

The Client-Server edition is used for larger installations of Lucullus, where different labs are using the software. This distributed architecture allows the data to be stored in a safe location while the front end user interfaces are located near the bioreactors where they need to be. Data can be reviewed in the offices by a direct link to the data server in the network. Data from different laboratories can be compared and can be used for process control or for reporting and making decisions on the path for further process development.



| Enterprise Edition

For even larger installations with Lucullus installations at different site (even in different countries) the Enterprise edition can be used. This version connects different installations of Lucullus and allows in the fly conversion and translation of process data. When authorized the user can view and compare data between different sites. This could be a production site and a process development site, or could even be different development sites in different locations working on the same process.



General Linux, Windows 7 (64-bit) Communication drivers include Inv., Windows 7 (64-bit) Communication drivers include my-Control, in-Control, ez-Control, i-Control, SUB-Control Optional drivers no Sartorius controllers, NBS controllers, Infors Controllers, Siemens PLC, TAP AMBR, Shaker/Incubstors Design of Experiments no no yes yes Media preparation planning no no no yes yes Analysis planning (reactors) no no no yes yes Resource planning (reactors) no no no yes yes Material Management no no no no yes yes Lot preparation no no no yes yes Storage management no no no yes yes Data Aquisition yes yes yes yes Process Control no yes yes yes Sampling planning and management no no yes yes	Operating system	See table					
Lite	Computer Hardware	no specific dema	no specific demands				
General Operating system Linux, Windows 7 (64-bit) Communication drivers include my-Control, in-Control, ez-Controll, F-Control, SUB-Control Optional drivers no Sartorius controllers, NBS controllers, Infors Controllers, Siemens PLC, TAP AMBR, Shaker/Incubators Design of Experiments no no yes yes Media preparation planning no no yes yes Analysis planning no no yes yes Resource planning (reactors) no no no yes yes Material Management no no no yes yes Lot preparation no no no yes yes Eilling no no no yes yes Storage management no no no yes yes Process Control no yes yes yes Monitoring and Alarms no yes yes yes Sampling planning and management no	Specifications	Lucullus	Lucullus	Lucullus	Lucullus		
Operating system Linux, Windows 7 (64-bit) Communication drivers include my-Control, in-Control, ez-Control, i-Control, SUB-Control Optional drivers no Sartorius controllers, NBS controllers, Infors Controllers, Siemens PLC, TAP AMBR, Shaker/Incubators Design of Experiments no no yes yes Media preparation planning no no no no yes Analysis planning (reactors) no no no no yes Resource planning (reactors) no no no yes yes Material Management no no no no yes yes Lot preparation no no no no yes yes Eilling no no no yes yes Storage management no no no yes yes Process Control yes yes yes yes Monitoring and Alarms no yes yes yes Sampling planning and ma		Lite	Standard	Advanced	Expert		
Communication drivers include my-Control, in-Control, ez-Control, i-Control, SUB-Control Optional drivers no Sartorius controllers, NBS controllers, Infors Controllers, Siemens PLC, TAP AMBR, Shaker/Incubators Design of Experiments no no yes yes Media preparation planning no no no yes yes Analysis planning (reactors) no no no no yes yes Material Management no no no no yes yes Lot preparation no no no no yes yes Filling no no no no yes yes Storage management no no no yes yes yes Process Control no no yes yes yes yes Process Control no yes yes yes yes Monitoring and Alarms no yes yes yes Data Retrieval from Analytica	General						
Optional drivers Design of Experiments No No No Yes Yes	Operating system	Linux, Windows	7 (64-bit)				
Design of Experiments no no no yes yes Media preparation planning no no no yes yes Analysis planning no no no no yes Resource planning (reactors) no no no yes yes Material Management no no no no yes Lot preparation no no no yes Storage management no no yes yes Process Control <td>Communication drivers include</td> <td>my-Control, in-Co</td> <td>ontrol, ez-Control, i-Cont</td> <td>trol, SUB-Control</td> <td></td>	Communication drivers include	my-Control, in-Co	ontrol, ez-Control, i-Cont	trol, SUB-Control			
Design of Experiments no no yes yes Media preparation planning no no no yes yes Analysis planning no no no no no yes yes Resource planning (reactors) no no no no no yes yes Material Management no no no no no no yes Lot preparation no no no no no yes Storage management no no no no yes yes Process Control no yes ye	Optional drivers	no	Sartorius controll	ers, NBS controllers, Info	ors Controllers,		
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Analysis planning no no no yes yes Resource planning (reactors) no no no yes yes Material Management no no no no yes Lot preparation no no no no yes Filling no no no no yes Storage management no no no no yes Storage management no no no no yes Process Control yes yes yes yes yes Monitoring and Alarms no yes yes yes yes Sampling planning and management no no yes Data Retrieval from Analytical Devices no yes yes yes Performance Analysis no yes yes yes yes Reporting no yes yes yes 21 CFR part 11 compliant no no no yes yes GAMP compliant yes yes yes Password protection no no yes yes User definable access rights	Design of Experiments	no	no	yes	yes		
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Material Management no no no yes Lot preparation no no no no yes Filling no no no no yes Storage management no no no yes Data Aquisition yes yes yes yes Process Control no yes yes yes Monitoring and Alarms no yes yes yes Sampling planning and management no no yes yes Data Retrieval from Analytical Devices no yes yes yes Interactive Data Analysis no yes yes yes Performance Analysis no no yes yes Reporting no no yes yes 21 CFR part 11 compliant no no yes yes 23 CFR part 11 compliant yes yes yes Yes yes yes	Analysis planning	no	no	no	yes		
Lot preparation no no no yes Filling no no no no yes Storage management no no no no yes Data Aquisition yes yes yes yes yes yes Process Control no yes yes yes yes yes Monitoring and Alarms no yes yes yes yes Sampling planning and management no no yes yes Data Retrieval from Analytical Devices no yes Interactive Data Analysis no yes yes yes Performance Analysis no no yes yes yes Reporting no yes yes yes 21 CFR part 11 compliant no no yes yes yes SAMP compliant yes yes yes yes Password protection no no yes yes yes Password protection no no yes yes yes User definable access rights	Resource planning (reactors)	no	no	yes	yes		
Filling no no no no yes Storage management no no no no yes Data Aquisition yes yes yes yes yes yes Process Control no yes yes yes yes yes Monitoring and Alarms no yes yes yes yes Sampling planning and management no no yes yes yes Data Retrieval from Analytical Devices no yes Interactive Data Analysis no yes yes yes Performance Analysis no no yes yes yes Reporting no yes yes yes 21 CFR part 11 compliant no no yes yes yes GAMP compliant yes yes yes yes ISA S88 standard no no yes yes yes Password protection no no yes yes yes User definable access rights	Material Management	no	no	no	yes		
Storage management no no no yes yes yes yes yes Process Control no yes yes yes yes yes yes yes yes Monitoring and Alarms no yes yes yes yes yes Sampling planning and management no no yes yes yes yes Data Retrieval from Analytical Devices no yes yes yes yes Performance Analysis no yes yes yes yes Reporting no yes yes yes yes yes ges Reporting no no yes yes yes yes yes ges 21 CFR part 11 compliant no no no yes yes yes ges GAMP compliant yes	Lot preparation	no	no	no	yes		
Data Aquisition yes yes yes yes yes Process Control no yes yes yes yes Monitoring and Alarms no yes yes yes yes Sampling planning and management no no yes yes Data Retrieval from Analytical Devices no yes Interactive Data Analysis no yes yes yes Performance Analysis no no yes yes yes Reporting no yes yes yes 21 CFR part 11 compliant no no yes yes GAMP compliant yes yes yes yes ISA S88 standard no no yes yes Password protection no no yes yes User definable access rights	Filling	no	no	no	yes		
Process ControlnoyesyesyesMonitoring and AlarmsnoyesyesyesSampling planning and managementnonoyesyesData Retrieval from Analytical DevicesnoyesyesInteractive Data AnalysisnoyesyesyesPerformance AnalysisnonoyesyesReportingnoyesyesyes21 CFR part 11 compliantnonoyesyesGAMP compliantyesyesyesyesISA S88 standardnononoyesyesPassword protectionnononoyesyesUser definable access rightsnononoyesyes	Storage management	no	no	no	yes		
Monitoring and Alarms no yes yes yes yes Sampling planning and management no no yes Data Retrieval from Analytical Devices no yes Interactive Data Analysis no yes yes Performance Analysis no no yes yes yes Reporting no yes yes yes yes 21 CFR part 11 compliant no no yes yes yes yes GAMP compliant yes yes yes yes yes yes ISA S88 standard no no yes	Data Aquisition	yes	yes	yes	yes		
Sampling planning and management no no yes yes Data Retrieval from Analytical Devices no yes Interactive Data Analysis no yes yes yes Performance Analysis no no yes yes Reporting no yes yes yes 21 CFR part 11 compliant no no yes yes GAMP compliant yes yes yes ISA S88 standard no no no yes yes Password protection no no yes yes User definable access rights no no yes yes	Process Control	no	yes	yes	yes		
Data Retrieval from Analytical Devices no yes Interactive Data Analysis no yes yes yes Performance Analysis no no yes yes yes Reporting no yes yes yes 21 CFR part 11 compliant no no yes yes GAMP compliant yes yes yes yes ISA S88 standard no no yes yes Password protection no no yes yes User definable access rights no no yes yes	Monitoring and Alarms	no	yes	yes	yes		
Interactive Data Analysis no yes yes yes Performance Analysis no no yes yes yes Reporting no yes yes yes 21 CFR part 11 compliant no no yes yes yes GAMP compliant yes yes yes yes yes ISA S88 standard no no yes yes yes yes Password protection no no yes yes yes yes User definable access rights no no yes yes yes	Sampling planning and management	no	no	yes	yes		
Performance AnalysisnonoyesyesReportingnoyesyesyes21 CFR part 11 compliantnonoyesyesGAMP compliantyesyesyesyesISA S88 standardnonoyesyesPassword protectionnonoyesyesUser definable access rightsnonoyesyes	Data Retrieval from Analytical Devices	no	yes				
Reporting no yes yes yes 21 CFR part 11 compliant no no yes yes GAMP compliant yes yes yes yes ISA S88 standard no no yes yes Password protection no no yes yes User definable access rights no no yes yes	Interactive Data Analysis	no	yes	yes	yes		
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GAMP compliant yes yes yes yes yes ISA S88 standard no no yes yes Password protection no no yes yes User definable access rights no no yes yes	Reporting	no	yes	yes	yes		
ISA S88 standard no no yes yes Password protection no no yes yes User definable access rights no no yes yes	21 CFR part 11 compliant	no	no	yes	yes		
Password protection no no yes yes User definable access rights no no yes yes	GAMP compliant	yes	yes	yes	yes		
User definable access rights no no yes yes	ISA S88 standard	no	no	yes	yes		
	Password protection	no	no	yes	yes		
Auto start after power failure no no yes yes	User definable access rights	no	no	yes	yes		
	Auto start after power failure	no	no	yes	yes		

Specifications	Lucullus	Lucullus	Lucullus	Lucullus
	Lite	Standard	Advanced	Expert
Data management				
Data storage system	Oracle database	Oracle database	Oracle database	Oracle database
Minimum sampling frequency	1 second	1 second	1 second	1 second
Sample frequency selectable per parameter	yes	yes	yes	yes
Data reduction definable per parameter	yes	yes	yes	yes
Data export to Excel	yes	yes	yes	yes
Data export in ASCII format	yes	yes	yes	yes
Graph export in graphics format	yes	yes	yes	yes
Dynamic Data Link to other programs	no	yes	yes	yes
On-line calculations				
using on-line and off-line data	no	yes	yes	yes
Data display				
Line graphs	yes	yes	yes	yes
Maximum number of pens per graph	8	8	8	8
Synoptic	no	yes	yes	yes
Procedure flow chart	no	yes	yes	yes
Combination of current and				
historic data in graphs	yes	yes	yes	yes
Combination of different				
active batches in graphs	yes	yes	yes	yes
Measured data table display	yes	yes	yes	yes
Scatter plots	yes	yes	yes	yes
Storage of predefined graph settings	yes	yes	yes	yes
C				
Supervisory control Programming of time based actions	no	VOS	VAS	VOS
Programming of event based actions	no	yes	yes	yes
Profiling of setpoints		yes	yes	yes
Manual setting of local control setpoints	no	yes	yes	yes
Recipe definition	no	yes	yes	yes
Troope definition	TIO	yes	yes	yes
Other				
Notebook for process and				
equipment remarks	yes	yes	yes	yes
equipment remarks Event viewer for system comments	yes	yes yes	yes yes	yes yes

DO₂ Sensors

Measurements of dissolved oxygen (DO₂) in biotechnological processes is a basis for process optimization and allows to maximize the product yield. A microorganism or cell responds to the oxygen concentration in regulating its overall metabolism. Therefore the knowledge of the DO₂ concentration and the proper control during the process are of great importance. The AppliSens DO2-sensor is specifically designed for long-term, stable and accurate measurements in bioprocesses. The DO₂-sensor has a titanium membrane module to minimize the measurement drift. The autoclavable polarization module allows polarizing of your DO₂-sensor while autoclaving your bioreactor system, resulting in reduced start-up time for your culture.

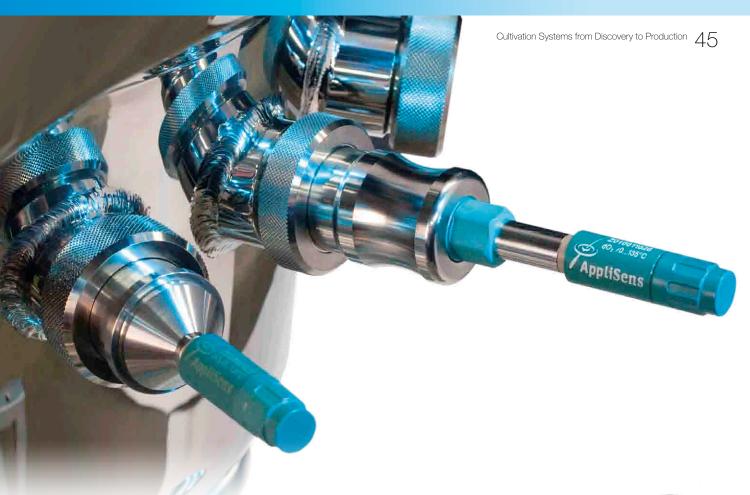
Features

- Titanium and PEEK materials guarantees low drift
- cGMP compatible by using FDA approved materials
- Electropolished surface roughness finish of 0.4 µm eases cleaning
- Short response time
- Withstands repeated SIP and CIP cycles
- Standardized PG 13.5 connection guarantees interchangeability with other bioreactor brands

Applications

- Microbial cultures
- Cell cultures
- Batch
- Fed Batch
- Continuous cultures
- Perfusion cultures





Optimum pola	arization potential	- 800 mV @ 40°C				
Polarization p	otential amplifier	- 675 mV				
Max. pressure	where linearity is guaranteed	4 bar				
Max. sterilizat	tion temperature	135°C				
Minimum pola	arization time	30 minutes				
Minimum pola	arization time after autoclaving	4h				
Optimum pola	arization time after autoclaving	Overnight				
Polarization c	urrent	Air / 25 °C / 1.013 bar / 100 % RH	(33 - 66) nA			
Polarization c	urrent	Air / 40 °C / 1.013 bar / 100 % RH	(65 - 98) nA			
Polarization c	urrent	O_2 / 40 °C / 1.013 bar / 0 % RH	(300 - 350) nA			
Response tim	e gas phase 20 °C	t (90%)	(20 - 30) s			
Response tim	e gas phase 40 °C	t (90%)	(10 - 20) s			
Response tim	e gas phase 60 °C	t (90%)	(5 - 10) s			
Drift between	15h - 5 days	< 0.2 % / day				
Drift between	5 days and 7 days	< 0.1 % / day				
Drift between	7 days and 30 days	< 0.05 % / day				
Insertion leng	th ø 12 mm sensors:					
Z010011025	insertion length 110 mm, 215 mm	total length (used with Tracfix sensor	holder)			
Z010015420	insertion length 154 mm, 259 mm	nm total length				
Z010023525	insertion length 235 mm, 340 mm	5 mm, 340 mm total length (Bioreactor 1-5 L)				
Z010032525	insertion length 325 mm, 430 mm	430 mm total length (Bioreactor 7 L)				
Z010042525	insertion length 425 mm, 530 mm	insertion length 425 mm, 530 mm total length (Bioreactor 15 L)				
Z010059025	insertion length 590 mm, 695 mm	length 590 mm, 695 mm total length (Bioreactor 20 L)				
Insertion leng	th ø 8 mm sensors:					
Z010015080	insertion length 150 mm					
Z010017080	insertion length 170 mm					





pH Sensors

In the biotech- and pharmaceutical industry it is vital to have precise information about the pH value of the bioprocess. The pH level directly affects viability, productivity, stability of the cells and it influences analysis of active ingredients.

The AppliSens pH+ sensor is specifically designed for long-term, stable and accurate measurements in bioprocesses. The pH+ sensor has a fixed sleeve diaphragm that reduces the influence of the culture medium on the pH measurement.

Compared to classic diaphragm types, the sleeve diaphragm increases measuring accuracy and increases the lifetime of the sensor which is vital for long lasting biotech cultivation processes.

Features

- Robust design by using tempered glass shaft
- Sensor head uses minimal space on bioreactor topplate
- Accurate measurement
- Low sensitivity to fouling due to sleeve diaphragm
- Stable signal over longer time
- FDA approved materials
- Withstands repeated SIP and CIP cycles
- Standardized PG 13.5 connection guarantees interchangeability with other bioreactor brands

Applications

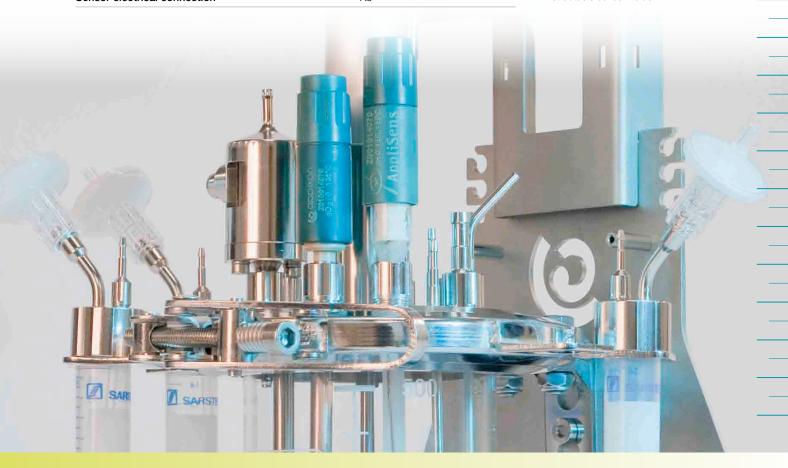
- Microbial cultures
- Cell cultures
- Batch
- Fed Batch
- Continuous cultures
- Perfusion cultures



Parameter	As Delivered
pH range	0 - 12 pH
Temperature range	0 - 135°C
Electrode zero point (E7)	+/-15 mV
Electrode slope (S4/7)	> 98%
Isothermal Intersection- pH (Eiso)	6.5 - 8
PH Range	4 - 9
Membrane resistance @ 25°C (ohm)	<1200
Membrane resistance @ 37°C (ohm)	<500
Calibration drift in Buffer 9 (mV / min)	< 2
Stirring Error (Buffer 9 @ 25 °C - pH)	< 0.05
Drift 72 hours after Autoclaving pH	< 0.13
Zero-point drift per week in PBS (pH)	< 0.05
Response Time (pH 9 to 4 @ 25 °C in	Seconds) < 90
Response Time 90% (pH 9 to 4 @ 25°	C in Seconds) < 45
Response Time (pH 9 to 4 @ 37°C in S	Seconds) < 45
Response Time 90% (pH 9 to 4 @ 37°	C in Seconds) < 45
Insertion length ø 12 mm sensors:	
Z001012051 insertion length 120 mn	n, 170 mm total length (used with Tracfix sensor holder)
Z001023551 insertion length 235 mn	n, 285 mm total length (Bioreactor 1-5 L)
Z001032551 insertion length 325 mn	n, 375 mm total length (Bioreactor 7 L)
Z001042551 insertion length 425 mn	n, 475 mm total length (Bioreactor 15 L)
Z001059051 insertion length 590 mn	n, 640 mm total length (Bioreactor 20 L)
Insertion length ø 8 mm sensors:	
Z001015080 insertion length 150 mn	າ
Z001017080 insertion length 170 mn	1
Sensor electrical connection	K9



pH Sensor in TracFix retractable sensor holder



iLine F, In-Line Smart Cell Culture Monitoring

The iLine Fast brings real-time label free monitoring to suspension mammalian cell bioreactors. The iLine F takes holograms of the cells and through advanced image analysis software, the cell count, cell size distribution, cell viability and parameters are generated automatically during the cultivation.



The iLine fast is designed specifically for use in combination with bioreactors. The technology can track a full cycle and can count cell viability from very low to high concentrations. The iLine Fast can be used in various settings and can be integrated with the bioreactor control systems.



The iLine Fast is connected to bioreactors via a specific, sterile closed loop disposable fluidics system. Cells are pumped out of the bioreactor, via an innovative pumping system, flow through the imaging device in a temperature-controlled environment and flow back to the bioreactor after the holograms of the cells have been captured. The holograms are continuously analyzed to compute cell density and cell viability.

Thanks to its on-line features, the technology strongly improves productivity and quality and allows staff in charge of the bioprocess environment to focus on tasks not linked to sampling, staining and analyses of data.

The monitoring platform is used continuously throughout the cell multiplication cycle and gives very accurate information related to the ideal harvest time of the culture.

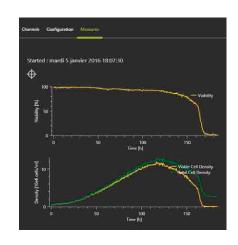


Cell density and viability

Cell viability and density are indicated via a simple visual gauge. For more in depth knowledge, Individual cells can be observed and analyzed via an easy to use cell browser. Green dots represent living cells, red dots represent dead cells and yellow dots represent cells within an aggregate.

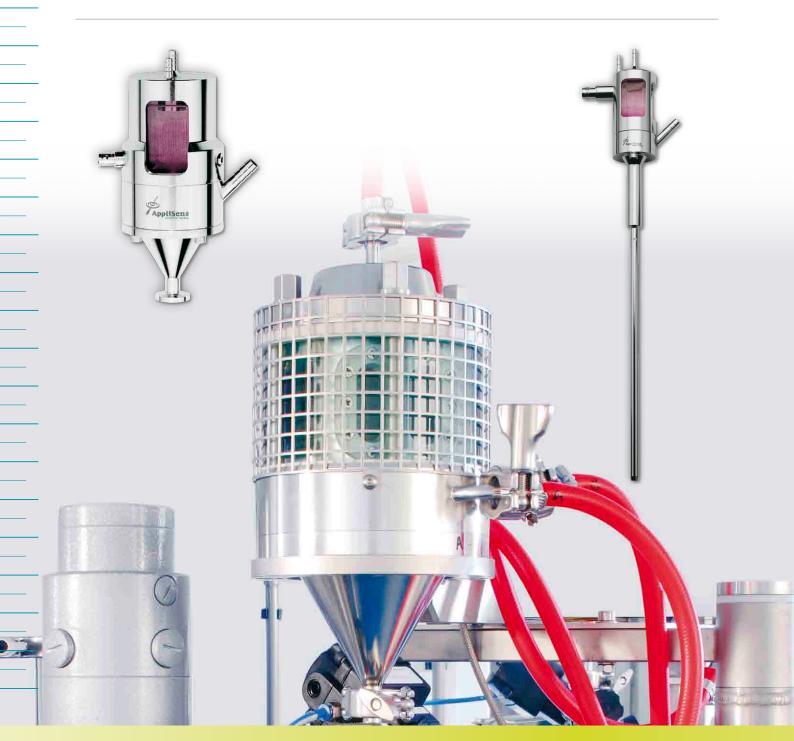
Cell density and viability are measured by using a label free method based on the 'holographic' fingerprint of a cell. First of all the iLine Fast captures holograms of all the cells flowing through the fluidics system in a 3D volume. In a second phase all objects within the observed volume, typically 100 times larger than traditional microscopes, are refocused. In a third step the holographic fingerprint of each cell is computed. The fingerprint is computed by an expert system and is based on a combination of parameters that allow for a fast and accurate classification. The methodology used by the quantitative imaging based platform can distinguish living and death cells and can eliminate debris easily making it a versatile and cost effective solution.

The iLine Fast has been benchmarked and compared to existing manual and automated off-line methods and has shown to be more consistent and accurate.

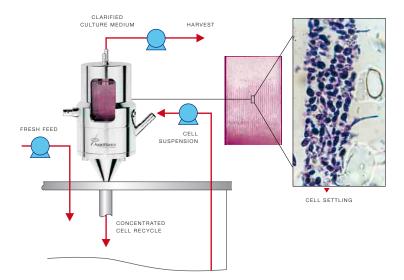


BioSep, acoustic cell retention system

The Applikon BioSep system is a unique, cell retention device for high-density perfusion processes. Using high frequency resonant ultrasonic waves to separate cells instead of a physical mesh or membrane, it offers all the benefits of traditional devices but without their inherent problems and limitations. The BioSep, based on the technology of acoustic resonance, is a non fouling / non clogging retention system. The BioSep can be applied in both R&D (max. 1 L/day), process development and on production scale (1000 L/day).



Typical configuration of acoustic cell retention system



Features

- Proven under cGMP conditions
- Easy to install and to operate
- Can be used in combination with any brand of bioreactor
- Long term cultivation possible (> 6 months)
- No fouling or blocking
- No damage to the cells
- High separation efficiency (> 95%)

Applications

- Cell cultures
- · Perfusion cultures.

BioSep system	1L	10L	50L	200L	1000L
Maximum perfusion rate	1 L/day	7 L/day	45 L/day	200 L/day	1000 L/day
Minimum perfusion rate	0.1 L/day	0.7 L/day	4.5 L/day	20 L/day	100 L/day
Separation efficiency	Up to 99% (depe	ending on cell cond	centration and perf	usion flow)	
Minimum cell concentration	2 x 10 ⁵ cells/ml (depending on cell	size)		
Bioreactor connection	6 mm OD tube	12 mm OD tube	Mounted	Mounted	Mounted
			separately	separately	separately
Medium inlet	3 mm hosebarb	6 mm hosebarb	10 mm hosebarb	0.5" TC	0.5" TC
Return line to bioreactor	3 mm hosebarb	6 mm OD	0.5" TC	0.5" TC	0.5" TC
		diptube			
Perfusion outlet	3 mm hosebarb	6 mm hosebarb	6 mm hosebarb	0.5" TC	0.5" TC
Weight	0.1 kg	0.5 kg	1.5 kg	13 kg	70 kg
Resonator volume	0.7 ml	7 ml	50 ml	290 ml	1450 ml

APS 995	APS 990	APS 990	APS 992	APS 993
15 Watt	150 Watt	150 Watt	350 Watt	1500 Watt
Combined with	305x130x130	305x130x130	450x400x135	450x300x450
my-Control				
Combined with my-Control	3.5	3.5	17.6	43
	15 Watt Combined with my-Control Combined with	15 Watt 150 Watt Combined with 305x130x130 my-Control Combined with 3.5	15 Watt 150 Watt 150 Watt Combined with 305x130x130 305x130x130 my-Control Combined with 3.5 3.5	15 Watt 150 Watt 150 Watt 350 Watt Combined with 305x130x130 305x130x130 450x400x135 my-Control Combined with 3.5 3.5 17.6

Bench scale and Pilot plant steam-in-place bioreactor systems

Applikon's concept of modularity (using standard modules to customize the functions of the bioreactor) is extended to the stainless steel pilot plant bioreactors as well. For scale up purposes the range of the Bio Bench and Pilot Systems, designed and built to the latest standards on hygienic processing and cGMP and GAMP validation requirements, complements the laboratory scale bioreactor systems. Scale-up from laboratory scale to pilot plant and small scale production is simplified by the consistent bioreactor design and the scalable control solutions. All systems are designed to be cleaned-in-place. Applikon offers CIP systems ranging from fully manual control to fully automated. Standardized bioreactor systems are available up to 140 liter total volume and custom build units can be supplied up to 2,000 liter total volume.

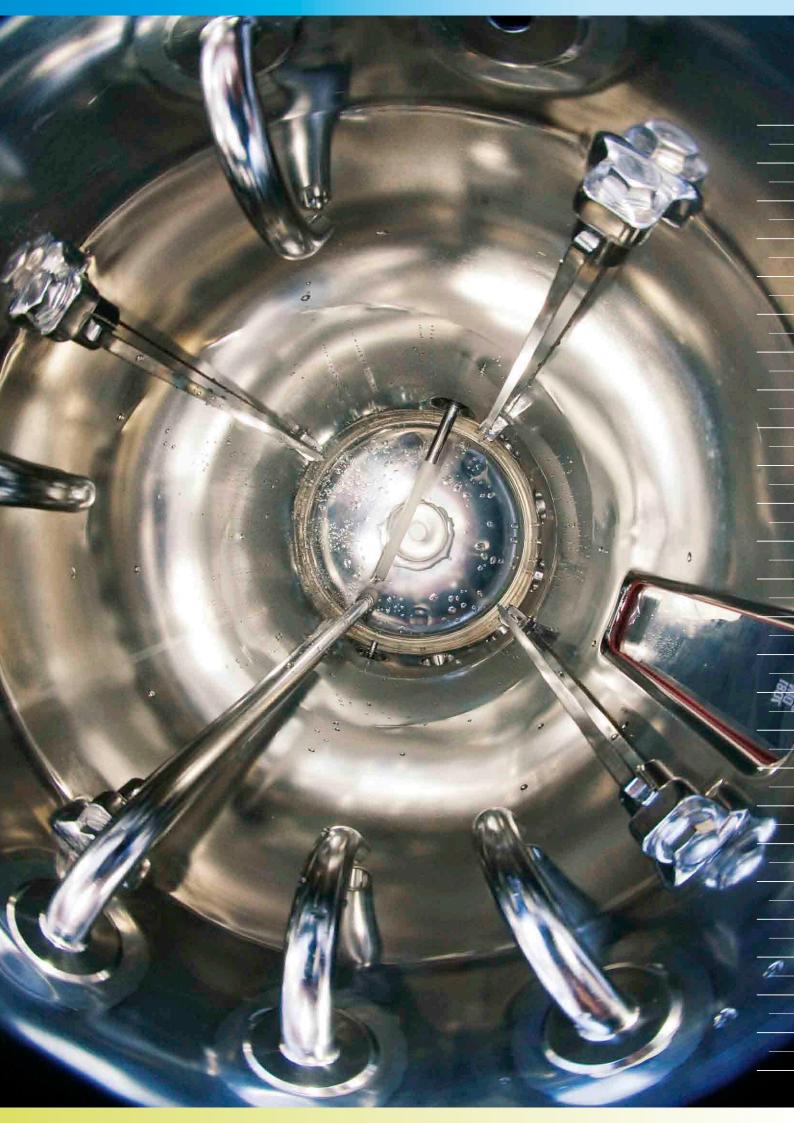
Features

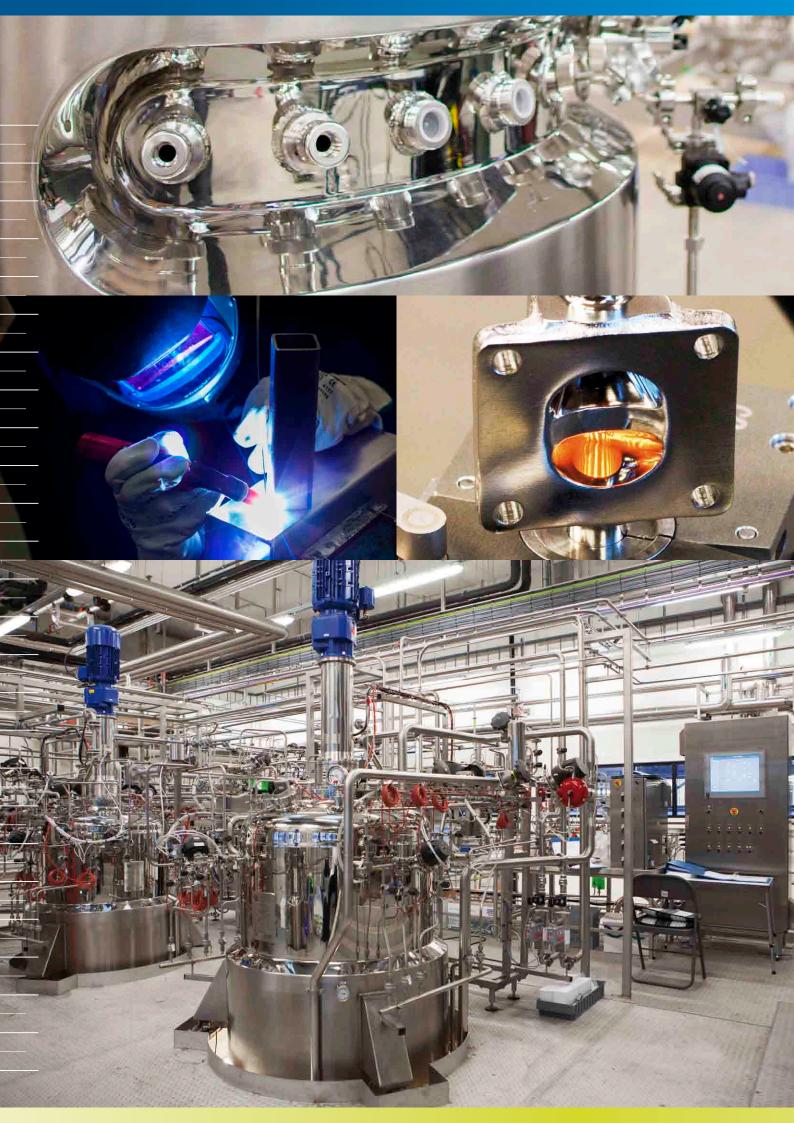
- Easy to clean mirror polished external finish
- Electropolished finish of all parts in contact with the culture (Ra < 0.4 μm) to allow efficient clean-in-place
- Modular design allows easy adaptation to changing process demands
- Magnetically coupled agitator for peace of mind
- cGMP compliant design simplifies validation
- Compact design reduces floor space needed
- Open frame construction gives easy access for maintenance and operation

Applications

- Scale-up studies
- Medium optimization
- Process optimization
- Small scale production
- · Microbial and Cell culture
- Batch, Fed-Batch, Perfusion and Continuous cultivation







	Total volume (liter)	Working volume (liter)	Minimum working volume (liter)	Aspect ratio total volume	Aspect ratio working volume		
7 liter Bio Bench	7	5	2	2.2	1.5		
15 liter Bio Bench	15	10	4	2.1	1.4		
20 liter Bio Bench	20	15	4	3.0	2.2		
30 liter Bio Bench	30	22.5	7	2.0	1.6		
30 liter Pilot Cell	30	20	7.5	1.5	1.0		
60 liter Pilot Cell	60	40	10	1.5	1.0		
130 liter Pilot Cell	130	100	28	1.5	1.0		
20 liter Pilot Microbial	20	15	4	3.0	2.2		
40 liter Pilot Microbial	40	30	7.5	3.0	2.2		
70 liter Pilot Microbial	70	50	10	3.0	2.2		
140 liter Pilot Microbial	140	100	20	3.0	2.2		
Custom build bioreactor systems are av	ailable up to 2000 lite	er total volume					
Drive system	Magnetically coupled, optional mechanical seal, bottom or top mounted						
	agitator for microbial cultures and top mounted for cell cultere systems						
Maximum agitator tipspeed (m/s)	5 m/s for microl	bial cultures and 1	m/s for cell cultures				
Impellers	Rushton and marine with outside diameters 0.33 - 0.5 vessel diameter						
Gas sparger	Porous sparger, L-Sparger or Ring-type sparger						
Gas overlay	Optional gas overlay line						
Exhaust gas	Water cooled exhaust gas condenser with internal spiral and/or jacketed						
Sampling	Optional resterilizable sample system in DN25 port in lower side wall						
Draining	Resterilizable bottom mounted bellows drain						
Additions	Sterilizable additions (push valves) and resterilizable addition ports						
pH	Measurement:	12 mm classic pH s	sensor in DN25 port	in lower side wa	II		
	Control: via acid	d pump or CO ₂ gas	(rotameter or MFC)	in combination v	vith alkali pump		
DO ₂	Measurement: 12 mm polarographic DO_2 sensor in DN25 port in lower side wall						
	Control: via a combination of N2, Air, O2 (Rotameter or MFC) and agitation or						
	nutrient addition pump						
Temperature	Measurement: Pt-100 sensor in in DN25 port in lower side wall						
	Cultivation control: cooling and heating jacket via bioreactor wall						
Foam	Measurement: Height adjustable conductivity based foam sensor						
	Control: Anti foa	am addition pump					
Level	Measurement: Height adjustable conductivity based level sensor or						
	loadcells in bioreactor frame						
	Control: pump for liquid addition or removal						



Special projects, customized solutions

Some customer demands cannot be fulfilled with our standard product offerings. In these cases we build custom solutions for our customers. These projects can range from very special mini bioreactors to a complete line of cGMP production systems ranging up to several thousand liters volume systems.



Key to the success of these projects is our experience of over 35 years building customized bioreactor solutions in combination with clear communication between our project team and the customer. We have developed special web based tools for communication and open information exchange within the project team. This ensures that everybody is working with the same up-to-date information all the time. The result of this approach is a customized bioreactor system that is delivered on time and completely according to the customer's specifications.

Over the past years we have generated a large library of customized solutions for a variety of specific demands. This guarantees that we can supply our customers with a proven solution for virtually any process demand. Since we are standardized on supplying products for the pharmaceutical industry, all our products and processes are fully documented. Our ISO 9001 certificate underlines the high quality level of our work and accompanying documentation.

AppliCare, total process control

What separates our service engineers from other organizations is that our people are BioProcessing Specialists. This means that not only do we know how to maintain and repair equipment, we can also troubleshoot because we understand process control. We specialize in bioreactors, controllers, software, motors, probes and all phases of your specific system's operation. Applikon's AppliCare will fix your problems - guaranteed. We help to eliminate the lost hours incurred to your production schedule and the high costs of downtime.

Installation and training

A correctly installed system, with comprehensive on-site training minimizes set-up time and ensures optimum operation within the shortest timeframe.

The installation service incorporates:

- Pre-plan design & Supply Service Requirement over-view before arrival of Applikon Equipment into your lab
- Connection of all tubing. hoses or piping from the Applikon Control Skid to the Supply Services or the Utility Panels
- Installation of all cabling from SCADA software to the controllers
- Site acceptance tests

Preventive maintenance

Downtime and emergency call-outs can be costly and always happen unexpectedly during an important run. Preventive maintenance extends the lifetime of the major components of your system, preventing premature wear and failure.

Benefits of Applikon's service agreements:

- Reduced charges for emergency repairs
- Free access to firmware upgrades
- · Reduced labour charges for any upgrade work or refresher training on site.

Extended warranty

This plan is a two-year extension of the original equipment warranty,

and includes parts and labor as needed.

Instrument calibration service

- Validation
- · Calibration certification



Offering a new breakthrough: Retrofitting

Make your old vessel new again

With the introduction of the i-Control, ez-Control and in-Control it is now possible to upgrade both Autoclavable and Steam in Place (SIP) vessels. Applikon service engineers are trained to make your old vessel not just new, but turn it into a powerful, yet intuitive, industrial unit. For a thorough inspection of your existing equipment, call Applikon for an appointment and our service engineer will visit your facility. After our Service Engineer details the specifications of your present system, Applikon will provide a comprehensive quote on time and cost analysis for the upgrade.

Other services offered

• Mass Flow Controller Verification

MFC Calibration on a yearly basis is very expensive & time consuming to a customer. AppliCare provides a service called MFC Verification which will indicate if the Flow Controller is within specifications and therefore no calibration would be necessary at the time of your Preventive Maintenance. This is done at a fraction of the cost of Standard calibration, in the security & safety of your own lab.

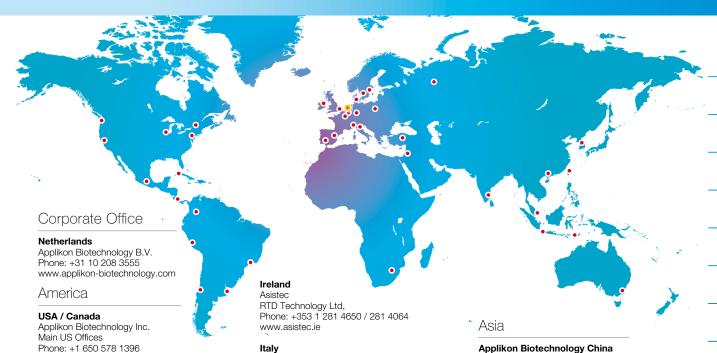
Technical phone support

Many times our service engineers can diagnose problems over the phone because they are trained to ask the insightful questions.

Spare parts

Stocking spare parts can be an expensive undertaking, especially when Applikon equipment is built with quality 25 years of quality. Applikon keeps the recommended spare parts of our standard systems in stock for quick deliveries.





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