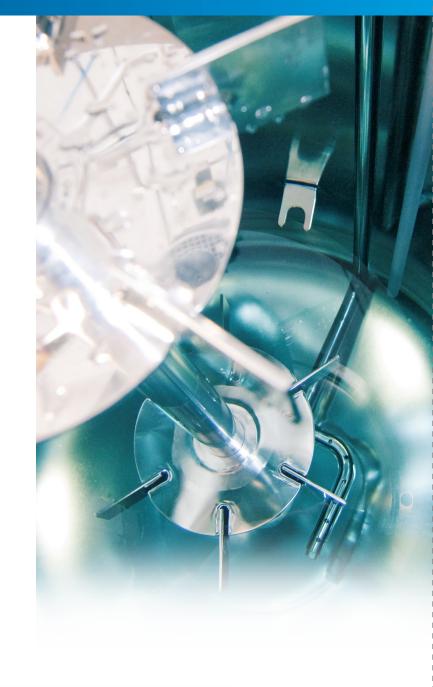


04	Micro-Flask	by Duetz
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- RamBio
- Alcohol Fermentation Monitor
- MiniBioreactors
- Glass autoclavable bioreactors
- Applikon PhotoBio
- AppliFlex Single Use Bioreactor
- BioBundle Cultivation Systems
- my-Control
- in-Control
- Ez-Control
- i-Control
- BioXpert®
- **36** DO<sub>2</sub> Sensors
- pH Sensors
- BioSep Retention system
- 42 Steam-In-Place Bioreactors
- Special bioreactor projects
- AppliCare







# 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 can take a customer from the initial screening stage up to full-scale production using the same platform. 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 relations 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 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 Schiedam, 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 20 countries.

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"



# 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.

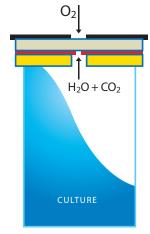
The Micro-Flask enables a single person to grow and test thousands of strains simultaneously with a minimum of repetitive handling.



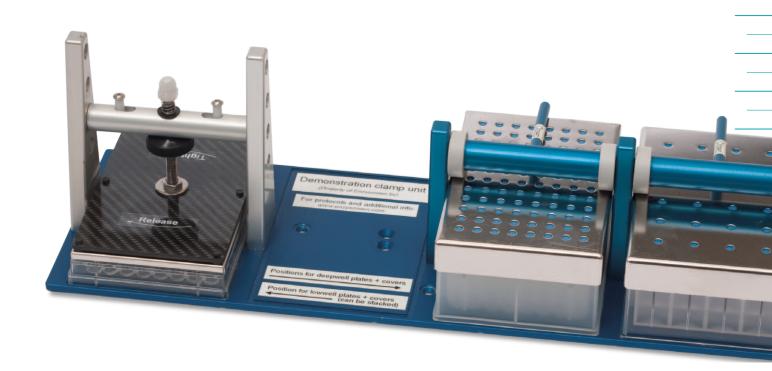
#### Features

- 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



Type of microtiter plate	Well volume	Culture volume	Orbital shaking frequency	Shaking amplitude	O <sub>2</sub> -transfer rate (30°C, air, 1 bar)	Headspace refreshment rate	Evaporation rate per well (at 30°C)	at 30	pattern 0 rpm ampl.   50 mm
24-square deep-well polypropylene, 17x17 mm, depth 40 mm	11000 µl	2500 µl 2500 µl 2500 µl 4000 µl 4000 µl	300 rpm 300 rpm 220 rpm 300 rpm 220 rpm	50 mm 25 mm 50 mm 50 mm 25 mm	$\begin{array}{c} 51 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 39 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 35 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 24 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 24 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \end{array}$	2.5 ml / min (1 VVM) 2.5 ml / min (0.6 VVM)	<b>50% humidity:</b> 50 µl H <sub>2</sub> O per day <b>75% humidity:</b> 25 µl H <sub>2</sub> O per day	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	$\begin{array}{c} 40 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 25 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 30 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 19 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \end{array}$	1.1 ml / min (1.4 VVM) 1.1 ml / min (1.1 VVM)	50% humidity: 30 $\mu$ l H <sub>2</sub> O per day 75% humidity: 15 $\mu$ l H <sub>2</sub> 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 <sub>2</sub> /I/h 12 mmol O <sub>2</sub> /I/h 24 mmol O <sub>2</sub> /I/h 7 mmol O <sub>2</sub> /I/h 18 mmol O <sub>2</sub> /I/h 3 mmol O <sub>2</sub> /I/h	1 ml / min (2 VVM) 1 ml / min (1.3 VVM) 1 ml / min (1 VVM)	<b>50% humidity:</b> 22 μl H <sub>2</sub> O per day <b>75% humidity:</b> 11 μl H <sub>2</sub> O per day	750 µl	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	$\begin{array}{c} 39 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 20 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 32 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 16 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 12 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \\ 12 \; \mathrm{mmol} \; \mathrm{O_2/I/h} \end{array}$	250 µl / min (2.5 VVM) 250 µl / min (1.7 VVM) 250 µl / min (1.3 VVM)	<b>50% humidity:</b> 6 $\mu$ I H <sub>2</sub> O per day <b>75% humidity:</b> 3 $\mu$ I H <sub>2</sub> O per day	150 µl	150 µl



# 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









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)

# Alcohol Fermentation Monitor, simple parallel cultivation

The Alcohol 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 CO<sub>2</sub>(g) 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  $CO_2(g)$  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 with XX mm outside diameter		
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		



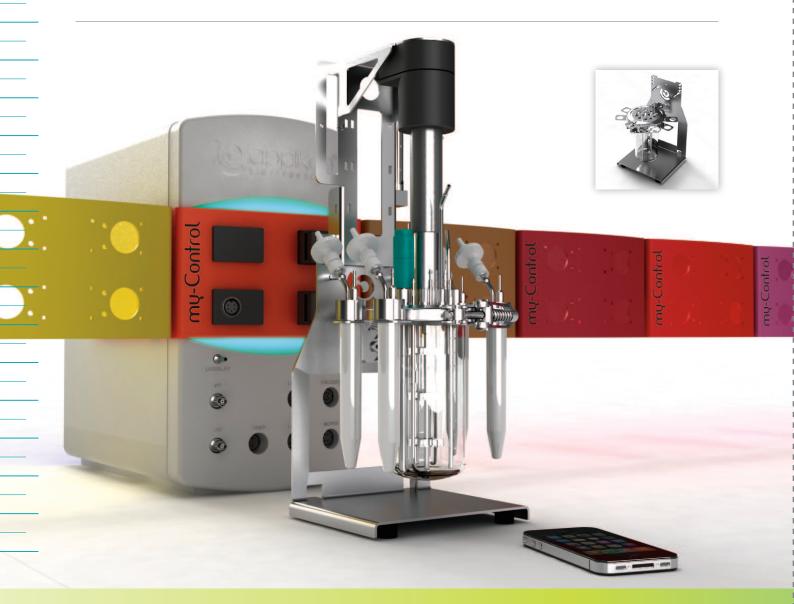
# Mini Bioreactors, real small... real bioreactors

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





	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				
Weight (kg)							
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	narine					
Gas sparger	Porous sparger or L-type	sparger					
Gas overlay	Yes						
Exhaust gas	Electrically cooled exhaust gas condenser (evaporation <3% per day at 37°C @ 2vvm)						
Sampling	Fixed sample pipe with optional sampling system						
Draining	Height adjustable drain pipe						
Additions	4 fixed inlet ports and optional micro liquid injectors						
Н	Measurement: 6 mm classic pH sensor						
	Control: via acid pump (variable speed pump)or CO <sub>2</sub> gas						
	in combination with alkali	in combination with alkali pump (variable speed pump)					
DO <sub>2</sub>	Measurement: 6 mm classic polarographic DO <sub>2</sub> sensor						
	Control: via a combination	Control: via a combination of N <sub>2</sub> , Air, O <sub>2</sub> (optional MFC)					
	and agitation or nutrient a	addition (variable speed pump)					
Temperature	Measurement: Pt-100 ser	Measurement: Pt-100 sensor in thermowell in topplate					
	Control: electrical cooling	Control: electrical cooling and heating jacket via bioreactor wall					
-oam	Measurement: Height adjustable conductivity based foam sensor						
	Control: Anti foam additio	n (variable speed pump)					
Level	Measurement: Height adji	ustable conductivity based lev	el sensor				
	Control: variable speed pu	ump for liquid addition or remo	oval				
Optional inlets	Septum, chemostat tube, liquid entry system						
Optional sensors	Biomass, Optical Density,	O <sub>2</sub> and CO <sub>2</sub> off gases.					



## 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 and
- · Continuous cultivation





	Total volume	Working volume	Minimum working	Aspect ratio total	Aspect ratio working		
	(L)	(L)	volume (L)	volume (L)	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		
	Internal Dia	meter (mm)	Internal Height (mm)	Autoclave di	mensions (WxH mn		
1 liter	95		200	!	ø172 x 393		
2 liter single wall	105		240	!	ø190 x 436		
2 liter jacketed	105		240	!	ø219 x 486		
3 liter single wall	130		240	!	ø190 x 436		
3 liter jacketed	130		240	!	ø235 x 436		
5 liter single wall	160		250	ø260 x 436			
5 liter jacketed	160		250	ø260 x 480			
7 liter single wall	160		350	ø260 x 600			
7 liter jacketed	160		350	ø264 x 645			
15 liter single wall	222		440	ø381 x 710			
15 liter jacketed	240		440	ø391 x 740			
20 liter single wall	222		620	!	ø381 x 900		
Drive system	Direct drive, I	ipsealed or magn	etically coupled				
Maximum stirrer speed (rpm)	Standard range is 50 – 1250.						
	1, 2 and 3 liter systems can be supplied with 2000 rpm motor						
Impellers	Rushton and marine with outside diameters 45mm, 60 mm 75 mm or 85 mm				mm		
Gas sparger	Porous sparger or L-type sparger						
Gas overlay	Yes						
Exhaust gas	Water cooled	l exhaust gas con	denser				
Sampling	Fixed height	or height adjustab	le sample pipe with optio	nal sampling sys	tem		
	Sample pipe	internal diameters	choices are: 1.7 mm, 4 r	mm, 6 mm or 10	mm		
Draining	Drain pipe						
Additions	Triple or singl	e inlet ports and o	pptional micro liquid inject	ors			
рН	Measuremen	t: 12 mm classic <sub>l</sub>	oH sensor				
	Control: via a	cid pump or CO <sub>2</sub>	gas (rotameter or MFC) ir	n combination wi	th alkali pump		
$DO_2$	Measurement: 12 mm classic polarographic DO <sub>2</sub> sensor						
	Control: via a	combination of N	$ m I_2$ , Air, O $_2$ (Rotameter or N	MFC) and agitatio	n or		
	nutrient addition pump						
Temperature	Measurement: Pt-100 sensor in thermowell in topplate						
	Control: cool	ing and/or heating	jacket via bioreactor wal	or via internal he	eat exchanger		
Foam	Measuremen	t: Height adjustab	le conductivity based foar	m sensor			
	Control: Anti foam addition pump						
Level	Measuremen	t: Height adjustab	le conductivity based leve	el sensor			
	Control: pum	p for liquid additio	n or removal				
Optional inlets	Septum, che	mostat tube, liquid	d entry system				

# Photo Bioreactors, the next best thing to sunlight

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 a photobioreactor with no downtime and minimal investment.

#### **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, (400-700nm), and Ideal for plant growth, to achieve better efficiency in the response of plants

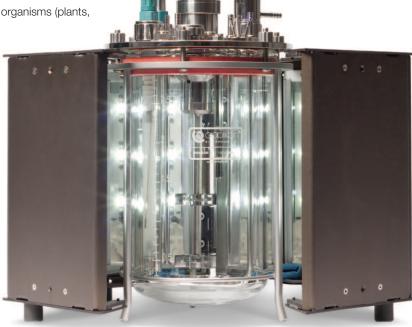
· Excellent wavelength stability over time, consistent, high-reliability

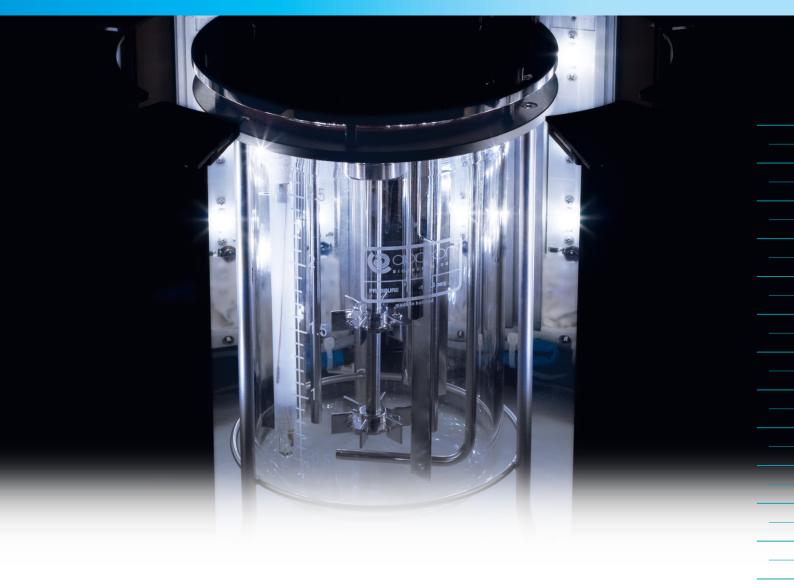
• Usable wavelength blue (470nm) and red (660nm) for plant growth

• 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).





140 watt of power or 24 light bank of 6 watt
8
0 to 100% PWM
Built in Real time clock
99:59 hours : minutes per step (maximum 9 time/intensity steps in one cycle)
Constant current source
IP-30 and IP-65 for Control Panel And IP67 for Light bank
16x2 Backlit LCD, Feather touch Keys
Full duplex RS232 or RS485 interface(optional)
0°C up to 60°C
115 / 230 V AC, 50-60 Hz
maximum 150 W

The PhotoBio range of bioreactors 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		
PhotoBioSU50	50 liter single use Appliflex rocking bioreactors	120 Watt panel		

# Single Use Bioreactors

Applikon offers two types of single-use bioreactors:

AppliFlex, bioreactors from 10 to 50 liter based on mixing by rocking motion and Bio-One, stirred tank bioreactors in the range of 50 to 2000 liter total volume. Both systems are unique in their accurate measurement and control of important process parameters. Both systems can be equipped with re-usable sensors and/or fluorophor pH and Dissolved Oxygen sensors. 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. Bio-One uses the Hy-Clone 50, 100, 250, 500, 1000 and 2000 liter bioreactors in combination with our ez-Control or i-Control process controllers. 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.

#### **Features**

- 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





	Appliflex		Bio-One			
Total volume	10 L, 20 L, 50 L		66 L, 120 L, 316 L, 660 L, 1320 L, 2700 L			
Working volume	5 L, 10 L, 25 L		50 L, 100 L, 250 L, 500 L, 1000 L, 2000 L			
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% O <sub>2</sub> saturation	0 12 pH	0 100% O <sub>2</sub> saturation	0 150°C	
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 @ 1 measurement	6 months	> 1 year	> 1 year	> 1 year	
	per minute					
	3.5 weeks @					
	1 measurement					
	per 2 minutes					

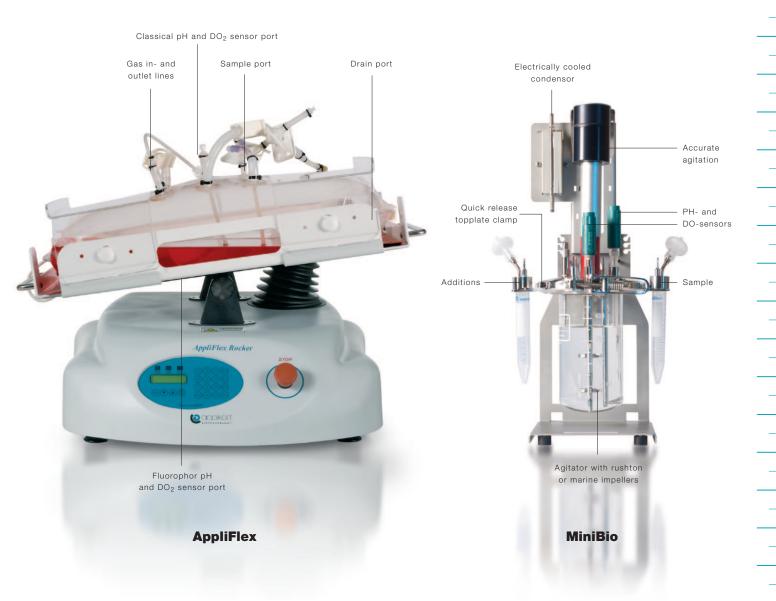
# BioBundle, complete cultivation systems

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 in 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 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, the product

	MiniBioBundle Cell Culture	MiniBioBundle Microbial	BioBundle Cell Culture	BioBundle Microbial	Appliflex 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	Lipsealed with	Lipsealed with	Lipsealed with	Lipsealed 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				
	optional	optional	optional	optional	optional
ρΗ	Measurement via				
	pH sensor control				
	via liquid alkali	via liquid alkali or	via liquid alkali	via liquid alkali and	via liquid alkali
	pump and CO <sub>2</sub>	acid addition pump	pump and CO <sub>2</sub>	acid addition pump	pump and CO <sub>2</sub>
	gas supply		gas supply		gas supply
Temperature	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				
	DO <sub>2</sub> sensor control	DO <sub>2</sub> sensor contro			
	via Air and $O_2$ gas	via Air supply and	via Air and O <sub>2</sub> gas	via Air and O <sub>2</sub>	via Air and O <sub>2</sub> gas
	supply	agitation speed	supply	supply and agitation	supply
				speed	
Foam	Option	Measurement via	Option	Measurement via	Option
		Foam sensor		Foam sensor	
		control via anti-foam	1	control via anti-foam	
		addition pump		addition pump	
_evel	Option	Option	Option		Option
iquid additions	4 fixed in topplate	4 fixed in topplate	3 ports in triple	3 ports in triple inlet,	One inoculum and
	and 1 septum port	and 1 septum port	inlet and one	one inoculum port	alkali inlet.
			inoculum port.	1 and septum port.	
	One liquid storage	Two liquid storage	One liquid storage	Three liquid storage	One liquid storage
	system included	systems included	system included	systems included	system included
Start-up kit	system included Included	systems included Included	Included	Included	Included

# my-Control, color your lab

my-Control is the most advanced bioreactor controller for small scale bioreactors starting at 50ml (working volume). The system can control bioreactors up to a total volume of 3L. 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 a 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 and to fit your laboratory.

#### **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 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)
Weight (kg)	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		
	pri, temperature, dissolved oxygen, agitation, toann and level		
	<ul> <li>Optional: biomass and fluorophor pH and fluorophor dissolved oxygen</li> </ul>		
	<ul> <li>Optional inputs 4 x analog in (0 – 10 V)</li> </ul>		
Control type	PID control with selectable autotuning adaptive control		
Actuators	8 x digital outputs for heating, cooling, fixed speed pump, solenoid valves etc.		
	<ul> <li>up to 4 Mass Flow Controllers or 4 solenoid valves for gas flow control</li> </ul>		
	<ul> <li>Spare I/O: 4 x analog out (0/4 – 20 mA)</li> </ul>		
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				
Agitation	0 - 1250 rpm	1 rpm		
	0 - 2000 rpm	1 rpm		
Analog in	8 x			
Analog out	4 x	4 x		
Digital in	8 x			
Digital out	8 x			
Fluorophor pH	optional 0.5 - 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	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-tuni	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	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"	
2Channel analog inputs	Range	4 – 20 mA	
	Accuracy	± 0.1% Full Scale value	
2Channel analog outputs	Range	4 – 20 mA	
	Accuracy	± 0.1% Full Scale value	
2Channel analog inputs for RTDs	Sensor Type	Pt-100	
	Range	-200°C+800°C	
	Accuracy	± 0.2 % Full Scale value	
	Resolution	0.1°C	





# BioXpert\*, supervisory control and data aquisition

BioXpert is a software tool to control bio-processes and to store the process data. The software is designed specifically for biotech researchers and operators in the bio-environment. The logical structure of the program and the user-friendly interface allows the program to be used by anyone. That is why over 3,000 copies of our BioXpert software are in use worldwide. The software is easy to operate and has extensive functionality for monitoring, collecting and storing data and controlling processes



Various BioXpert versions have been developed based on international standards for use in either research and pilot plant or production environments. BioXpert Lite is designed for data collection, data storage and data presentation. The research version (BioXpert 2) offers maximum flexibility to set up and to modify processes. The pilot plant and production version (BioXpert W7) focuses on process repeatability and data security.

#### Features

BioXpert seamlessly integrates with Applikon and other makes of controllers and peripheral equipment to enable you to get the maximum out of your cultivation system. Pre-defined recipes exist for microbial culture, mammalian cell culture and plant cell culture. All process data and controller data can be stored at user-defined intervals. Off-line measurements can be added to the process data to be used for calculations or advanced process control. BioXpert offers different ways of presenting your measured data trend graph, table and bar graph presentation. The on-line calculations of BioXpert can be used to calculate derived variables. The statement editor and interpreter allow time and/or event based execution of advanced control strategies. Another option for supervisory control is the use of timed profiles. Remote Access for BioXpert XP makes process data accessible for monitoring throughout a network using web browser technology.



## Applications

• BioXpert software can be used for Microbial and Cell cultures in Batch, Fed-Batch, Perfusion and Continuous cultivation

Specifications	BioXpert Lite	BioXpert 2	BioXpert W7
General			
Operating system	Windows NT,	Windows NT,	Windows XP (service pack 3)
	2000, XP, Vista,	2000, XP, Vista,	Vista
	Windows 7 (32 bit)	Windows 7 (32 bit)	Windows 7 (32 bit)
Communication drivers include	ADI 1010, ADI 1020,	ADI 1010, ADI 1020,	ADI 1010, ADI 1030,
	ADI 1030,	ADI 1030, ADI 1060	ADI 1060
	my-Control	my-Control	my-Control (via OPC)
	ez-Control	ez-Control	ez-Control (via OPC)
	in-Control	in-Control	in-Control (via OPC)
			i-Control (via OPC)
	AppliFlex Rocker	AppliFlex Rocker	AppliFlex Rocker
	Balances	Balances	
Additional drivers available separately	no	no	yes
	ADDA card	ADDA card	
Measurement of process values			
from process controllers	yes	yes	yes
Control of process setpoints in			
process controllers	no	yes	yes
Starting and stopping of control loops	no	yes	yes
Programming of local process			
controllers	no	no	yes
Reading of calibration data	no	no	yes
21 CFR part 11 compliant	no	no	yes
GAMP compliant	yes	yes	yes
SA S88 standard	no	no	yes
Password protection	no	no	yes
User definable access rights	no	no	yes
Auto start after power failure	no	no	yes



Specifications	BioXpert Lite	BioXpert 2	BioXpert W7
Data management			
On line data collection	yes	yes	yes
Off-line data collection	yes	yes	yes
Data storage system	Proprietary file format	Proprietary file format	SQL database
Minimum sampling frequency	1 minute	1 minute	1 second
Sample frequency selectable			
oer parameter	no	no	yes
Data export to Excel	yes	yes	yes
Data export in ASCII format	yes	yes	yes
Graph export in BMP format	yes	yes	
On-line calculations using			
on-line and off-line data	no	yes	yes
Data display			
ine graphs	yes	yes	yes
Bar graphs	yes	yes	yes
Synoptic	yes	yes	yes
Procedure flow chart	no	no	yes
Combination of current and historic			
data in graphs	yes	yes	yes
Combination of different active			
patches in graphs	yes	yes	
Measured data table display	yes	yes	yes
Scatter plots	yes	yes	yes
Storage of predefined graph settings	yes	yes	yes
Supervisory control			
Programming of time based actions	no	yes	yes
Programming of event based actions	no	yes	yes
Profiling of setpoints	no	yes	yes
Manual setting of local control set points	no	yes	yes
Recipe definition	no	yes	yes
Other			
Notebook for process and			
equipment remarks	yes	yes	yes
Event viewer for system comments	yes	yes	yes
Audit trail	no	no	yes
Batch reports supported	no	no	yes
Remote access	no	no	yes

## DO<sub>2</sub> Sensors

Measurements of dissolved oxygen (DO<sub>2</sub>) 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 DO<sub>2</sub> concentration and the proper control during the process are of great importance. The AppliSens Low Drift DO2-sensor is specifically designed for long-term, stable and accurate measurements in bioprocesses. The DO<sub>2</sub>-sensor has a titanium membrane module to minimize the measurement drift. The autoclavable polarization module allows polarizing of your DO<sub>2</sub>-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

- 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	rization 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 current		O2 / 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)					
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	ŋth						
2010011025 insertion length 110 mm, 215 mm total length (used with Tracfix sensor holder)							
Z010015420	insertion length 154 mm, 259 mm total length						
Z010023525	insertion length 235 mm, 340 mm total length (Bioreactor 1-5 Ltr.)						
Z010032525	insertion length 325 mm, 430 mm total length (Bioreactor 7 Ltr.)						
Z010042525	25 insertion length 425 mm, 530 mm total length (Bioreactor 15 Ltr.)						
Z010059025	insertion length 590 mm, 695 m	m total length (Bioreactor 20 Ltr.)					





# 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 (MΩ)	<1200
Membrane resistance @ 37°C (MΩ)	<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 Seconds)	< 45
Response Time 90% (pH 9 to 4 @ 37°C in Seconds)	< 45
Sensor diameter	12 mm
Sensor length, insertion length/total length	
Article nr:	
Z001012051	120/170 mm
Z001023551	235/185 mm
Z001032551	325/375 mm
Z001042551	425/475 mm
Z001059051	590/640 mm
Sensor electrical connection	K9



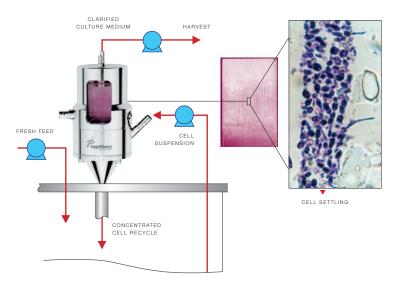


# BioSep, acoustic cell retention system

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. 1L/day), process development and on production scale (1000L/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 (>90 days)
- 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	Up to 99% (depending on cell concentration and perfusion flow)					
Minimum cell concentration	2 x 10 <sup>5</sup> cells/ml (	2 x 10 <sup>5</sup> 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		

BioSep Controller	APS 995	APS 990	APS 990	APS 992	APS 993
BioSep Controller Power	15 Watt	150 Watt	150 Watt	350 Watt	1500 Watt
BioSep Controller Dimensions	Combined with	305x130x130	305x130x130	450x400x135	450x300x450
(DxWxH, mm)	my-Control				
BioSep Controller Weight (kg)	Combined with	3.5	3.5	17.6	43
	my-Control				

# 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, comple-ments 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 2000 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

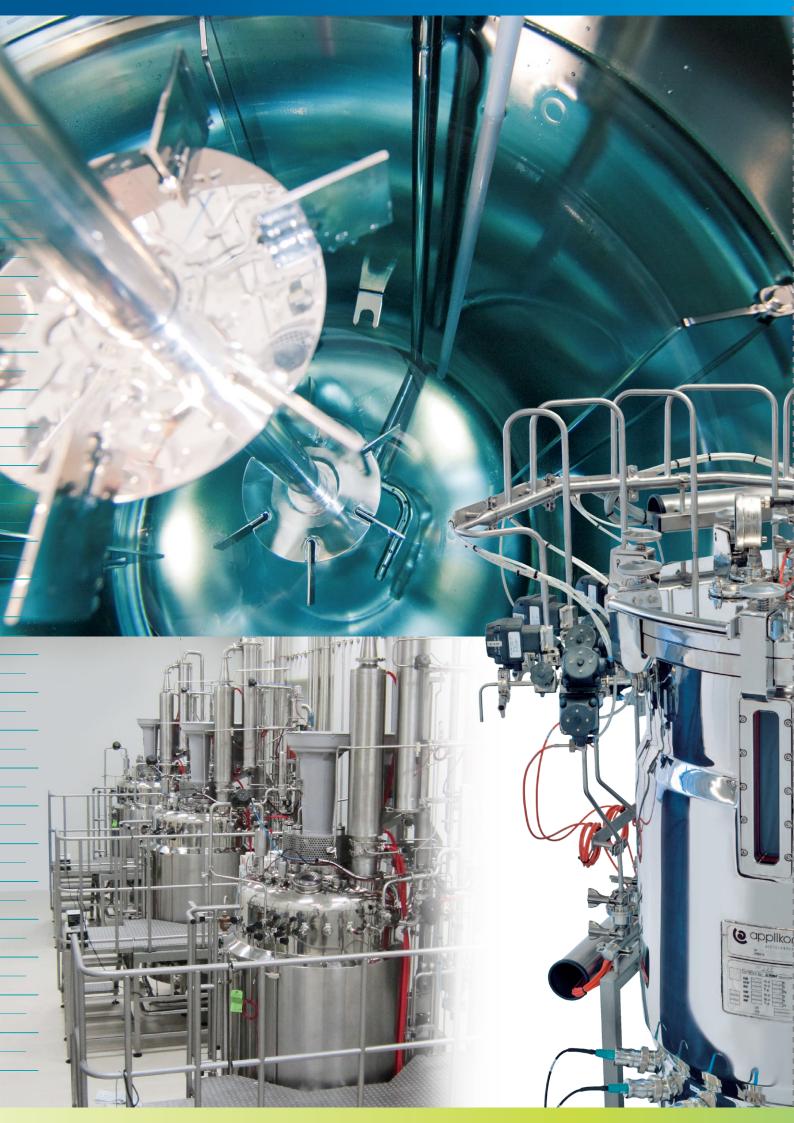
## **Applications**

- 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	Aspect	Aspect ratio working volume		
			working	ratio total			
			volume (liter)	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 a	ailable up to 2000 lite	er total volume					
Drive system	Direct drive, 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 microbial 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 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						
рН	Measurement: 12 mm classic pH sensor in DN25 port in lower side wall						
	Control: via acid pump or $\rm CO_2$ gas (rotameter or MFC) in combination with alkali pump						
DO <sub>2</sub>	Measurement: 12 mm polarographic DO <sub>2</sub> 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 foam addition pump						
Level	Measurement: Height adjustable conductivity based level sensor or I						
	oadcells 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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