

bioREACTOR

High-throughput bioprocess development in the milliliter scale

bioREACTOR

The 2mag bioREACTOR is a new developed, space-saving and user-friendly bioreaction block with up to 48 parallelized mini reactors.

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Advantages

- High parallelization
- Precise temperature control
- Optimal working volume
- Non-invasive real-time measurement of pH and DO
- Easy handling through disposables
- High oxygen transfer rates
- Automated stirrer monitoring
- Intelligent software for parallel operation of several bioREACTOR units
- Autoclavability and high sterility
- Easy upscaling
- Automatization
- High parallel and sequential reproducibility

The high parallelization allows an easy realization of high-throughput fermentations in the biotechnological, chemical or pharmaceutical research. This strongly reduces development time and costs for new production processes. Miniaturization into the low milliliter scale (8-15 ml) provides a significant saving of material and process costs.

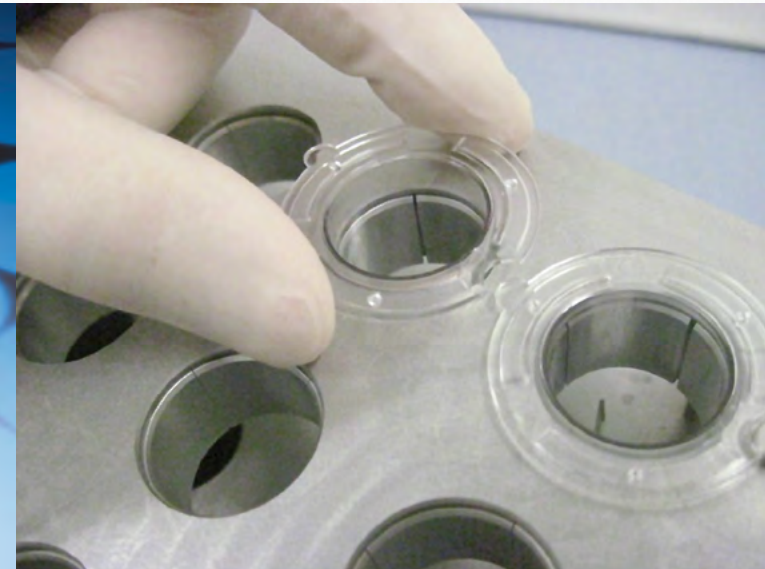
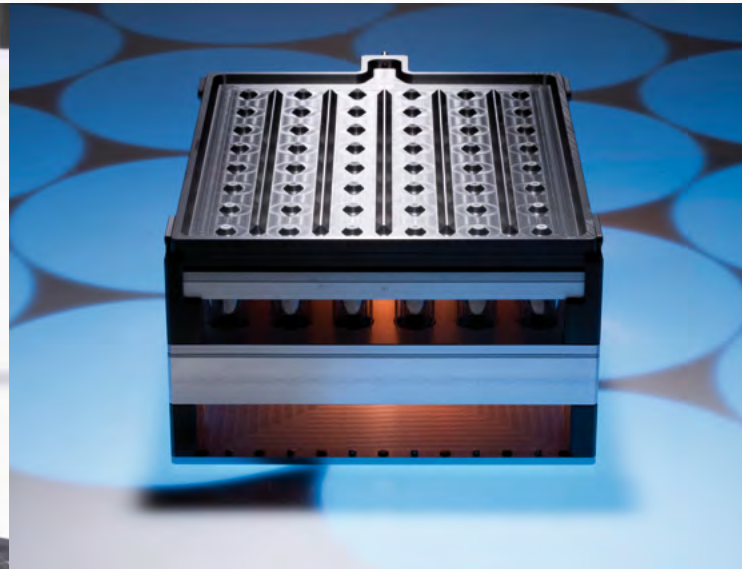
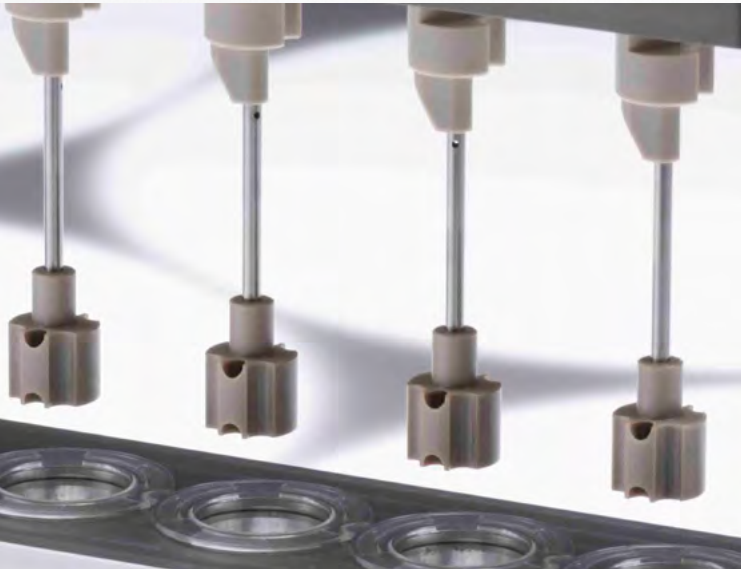
The 2mag bioREACTOR is characterized by a precise temperature control, an exactly controllable stirring speed with automatic stirrer monitoring as well as precise non-invasive real-time measurement of pH and dissolved oxygen (DO). Gassing and mixing of the reaction vessels is provided by the gas inducing, inductive stirring elements. The sterile head-space aeration prevents cross and external contaminations and allows cultivation of aerobic and anaerobic microorganisms.

An easy and secure scaling-up of the results into the production scale can be ensured by precisely defined engineering parameters and the comparable power and oxygen input ($k_L a > 0,4 \text{ s}^{-1}$) to well-established stirred tank reactors. The bioREACTOR can be operated as standalone or fully automated by integration into a pipetting robot.

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The 2mag bioREACTOR is featured by a high parallelization, a precise temperature control and an optimal working volume.

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Parallelization

The 2mag bioREACTOR is available in two model variants with 8 or 48 parallel reaction vessels. A still higher parallelization can be achieved by simultaneous use of several bioREACTOR units. These can be controlled via an intelligent central software and important process parameters (pH and DO) can be monitored in real-time. In addition, the simultaneous use of several bioREACTOR units allows the variation of other parameters e.g. the temperature or the stirring speed.

Temperature Control

The temperature of the bioreactor block is measured by an internal Pt100 sensor and controlled externally by a thermostat. To avoid evaporation loss, the headspace of the reaction vessels is cooled down with a reflux cooler. The evaporated water condenses and rests in the reaction vessels.

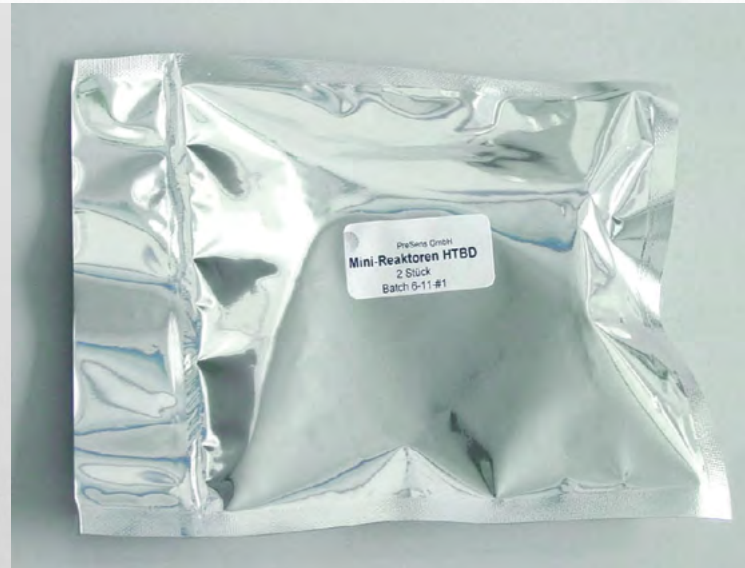
Working Volume

The working volume of the reaction vessels ranges between 8 and 15 milliliters. This allows repeated sampling without strong reduction of the fermentation volume but also enough capacity for adding pH correction agents or substrates.

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pH and dissolved oxygen can be measured over the whole process time with the sensor spot equipped disposable reaction vessels.

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Real-time measurement of pH and DO

pH and dissolved oxygen can be measured in real-time with a non-invasive optical sensor system over the whole process time. For this, the bottom of the reaction vessels are equipped with small sensor spots (pH and O₂ sensitive luminescent dyes). The fluorometric measurement is provided by stimulation with light and measurement of the decay time (DLR = Dual Lifetime Referencing Principle, PreSens GmbH). The measuring range lies between 6.0 and 8.5 for the pH and between 0 % and 50 % for the dissolved oxygen.

Reaction vessels (Disposables)

The spotted disposable reaction vessels are made of polystyrene and sterile packed in a set of two. This allows a time saving and easy handling of the bioREACTOR. The special geometry of the reaction vessels with baffles in combination with the used stirring elements lead to a very good mixing of the medium and to high oxygen transfer rates.

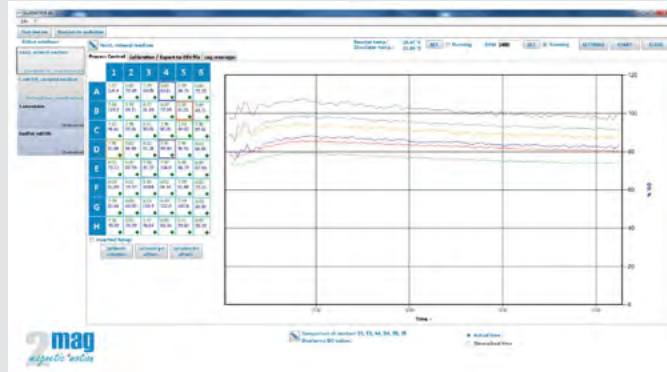
Gassing

The continuous gassing of the bioREACTOR can be realized with a gas mixing station. Depending on the used gases (O₂, N₂, CO₂, Air,...) aerobic and anaerobic cultivations are possible. The gas transfer into the medium of the reaction vessels is done passively through the gas inducing, inductive driven magnetic stirring elements. The gas transfer rate can be adjusted via the stirring speed.

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The integrated stirrer monitoring and the intelligent software allow a secure, sterile and simple operation of the 2mag bioREACTOR.

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Stirrer monitoring

At very high cell densities or a high percentage of solids in the medium a stop of rare stirrers can occur in less cases. This will be detected in a few seconds and the stirrers will be restarted automatically. Therewith, the stirrer monitoring guarantees a secure experimental run.

Intelligent software

The stand alone software allows the parallel use of several bioREACTOR 8 and/or 48 units. At the same time, already finished runs can be compared with new running experiments.

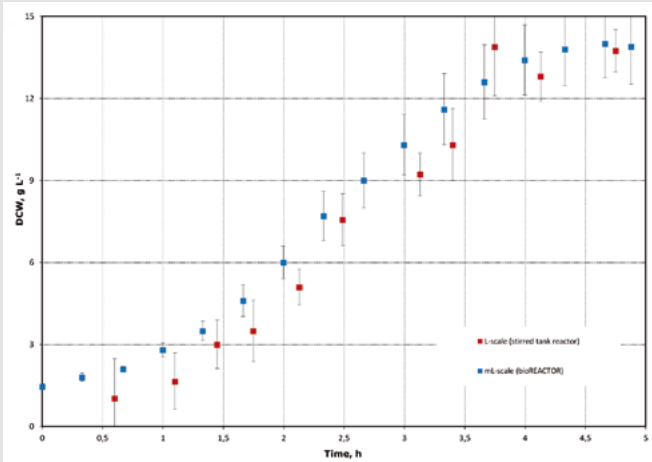
Autoclavability and sterility

All parts which can be in contact with the medium are autoclavable or sterile packed disposables. The gassing unit with the fixed stirring elements is completely autoclavable. In addition, the complete bioreactor block is sterilizable with ethanol. The disposable reaction vessels are sterile packed and were disposed after the experiment. During the experiment, the sterile headspace gassing avoids cross and external contaminations. Furthermore, an optional exhaust gas unit can avoid spreading of spores into the environment.

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The 2mag bioREACTOR can be used as standalone or fully automated by integration into a pipetting robot. The results are easy scalable into the laboratory and production scale.

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Scalability

The exactly defined geometry of the stirring elements, the precisely characterized process parameters as well as the to standard laboratory stirred tank reactors comparable power and oxygen input ($kLa > 0.4 \text{ s}^{-1}$) through the stirring elements allow an easy upscaling of the results into the laboratory and production scale.

Automatization

The bioREACTOR can be used as stand alone or fully automated by integration into a pipetting robot. The integration allows pH control, adding of substrates and taking samples out of the reaction vessels. Therewith feeding strategies can be analyzed, an online measurement of the optical density (OD) can be made or samples for additional tests can be taken out of the vessels.

Typ	bioREACTOR 48	bioREACTOR 8
Stirring points	48	8
Stirring point distance	35 mm	
Material block	Aluminium, hard-coated	
Dimensions (WxDxH)	240 x 340 x 145 mm	66 x 340 x 145 mm
Weight (gross)	approx. 16 kg	approx. 3.7 kg
Electrical data	230 V / 100 W	230 V / 50 W
Protection category	IP31	
Reaction vessels		
Working volume	8 - 15 ml	
Material	Polystyrene (PS)	
Temperature		
Operating conditions	+10 °C up to +65 °C (at 80% humidity)	
Mixing		
Stirring element	gas inducing stirring elements	
Stirring speed	100 - 4,000 rpm	
Gassing		
Gassing rate	4.8 l/min	0.8 l/min
Real-time measurement		
pH range	6.0 - 8.5	
DO range	0 - 50 % O ₂	
Response time (pH/DO)	< 30 s (at 15 - 45°C)	
Order No	B70048	B70008

2 years warranty on material and manufacturing. We reserve the right to make technical alterations. We do not assume liability for errors in printing or typing.

Delivery contents

bioREACTOR with control unit bioREACTORcontrol
 Accessories (maintenance tool, steriBOX)
 PreSens sensor system for non-invasive pH-/DO-measurement
 Standalone Software

Peripheral units e.g. thermostats, reflux coolers or gas mixing stations on request!

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Due to its versatility, the bioREACTOR was already applied in the development of various biotechnological processes. To realize many more processes the 2mag bioREACTOR is being developed further.

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Applications

- Aerobic and anaerobic cultivation of bacteria, yeasts and fungi
- Evaluation of adequate production strains (strain development)
- Media screening and optimization
- Optimization of the process design (manual batch or automated batch or fed-batch process design with pipetting robots)
- Cell growth experiments
- Studies of gene and protein expression
- Viability tests
- Inhibition and toxicity experiments
- Enzyme assays
- Quality control
- Also applicable for chemical and enzymatic reactions

Application examples

- Production of Vitamin B2 with *Bacillus subtilis* [1]
- Enzymatic hydrolysis of plant materials [2]
- Production of bio butanol with *Clostridium acetobutylicum* [3]
- Production of an antimycotic with *Streptomyces tendae* [4]
- Production of acetic acid from synthetic gas with *Acetobacterium woodii* [5]
- Feeding strategies of *Saccharomyces cerevisiae* [6]
- Production of hydroxyisobutyric acid with *Cupriavidus necator* [7]
- Fluxome analysis of *Escherichia coli* mutants [8]

Literature

- [1] Vester A, Hans M, Hohmann P, Weuster-Botz D (2009): Discrimination of riboflavin producing *Bacillus subtilis* strains based on their fed-batch process performances on a milliliter scale. *Appl Microbiol Biotechnol* 84: 71-76
- [2] Riedberger P, Weuster-Botz D (2012): New miniature stirred-tank bioreactors for parallel study of enzymatic biomass hydrolysis. *Bioresour Technol* 106: 138-146
- [3] Schmidt M, Weuster-Botz D (2012): Reaction engineering studies of acetone-butanol-ethanol fermentation with *Clostridium acetobutylicum*. *Biotechnol J* 7: 656-661
- [4] Hortsch R, Krispin H, Weuster-Botz D (2010): Process performance of parallel bioreactors for batch cultivation of *Streptomyces tendae*. *Bioproc Biosys Eng*, 34: 297-304
- [5] Demler M, Weuster-Botz D (2011): Reaction engineering analysis of hydrogenotrophic production of acetic acid by *Acetobacterium woodii*. *Biotechnol Bioeng* 108: 470-474
- [6] Gebhardt G, Hortsch R, Kaufmann K, Arnold M, Weuster-Botz D (2011): A new microfluidic concept for parallel operated milliliter-scale stirred tank bioreactors. *Biotechnol Prog* Vol. 27, No. 3.
- [7] Höfel T, Wittmann E, Reinecke L, Weuster-Botz D (2010): Reaction engineering studies for the production of 2-hydroxyisobutyric acid with recombinant *Cupriavidus necator* H16. *Appl Microbiol Biotechnol* 88: 477-484.
- [8] Heux S, Poinot J, Massou S, Sokol S, Portais JC (2014): A novel platform for automated high-throughput fluxome profiling of metabolic variants. *Metabolic Engineering* 25:8-19.

WELL-PROVEN CONCEPTS - INNOVATIVE PRODUCTS

2mag is providing you more than 40 years of competence in the conception, development, production and sales of magnetic and inductive drive concepts, as e.g. magnetic stirrers.

magnetic motion



Our experience paired with a great passion and emotion for our customers – and our products – enables the fast and economic creation of solutions precisely for your needs.

Ask us – test us – we are there for you!

- 100% wear- and maintenance-free
- 30% more stirring power than comparable systems
- Super-flat, space-saving stirring drives - ideal for robotics
- Synchronous speed at all stirring positions
- Made for permanent operations
- Made in Germany

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