

BioLector® Pro

Microfluidic Bioprocess Control

**m2p
labs**

32 Parallel Microbioreactors

pH Control

Continuous Feeding

Online Monitoring

Scalability



Full Bioprocess Control On-the-Plate

BioLector® Pro

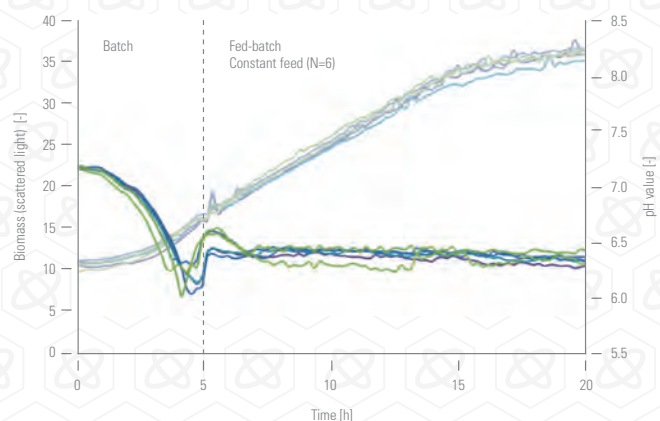
The BioLector® Pro is the first microbioreactor system combining the established BioLector® technology with an innovative microfluidic chip.

The system is based on a standard microtiter plate format and operates with non-invasive, optical sensors. The disposable 48 well microtiter plate of the BioLector® Pro features online measurements of biomass, fluorescence, pH and DO and simultaneously controls the pH and feeding rates through micro-valves and microfluidic-channels. For the first time, these unique microfluidic components allow continuous feeding and pH control in standard microtiter plates. There is no tubing and no liquid handling needed anymore; everything is part of the gamma radiated ready-to-use plate!

Applications

- Fed-batch development
- pH profiling
- Feeding rate optimization
- Media screening and optimization
- Fermentation parameter optimization
- Cell line and strain screening
- Anaerobic and microaerophilic fermentations
- Synthetic and systems biology
- Statistical design of experiments (DoE)
- Growth characterization
- High-throughput protein expression
- Enzyme and cell activity tests
- Functional genomics
- Proteomic studies
- Inhibition and toxicity tests
- Quality control

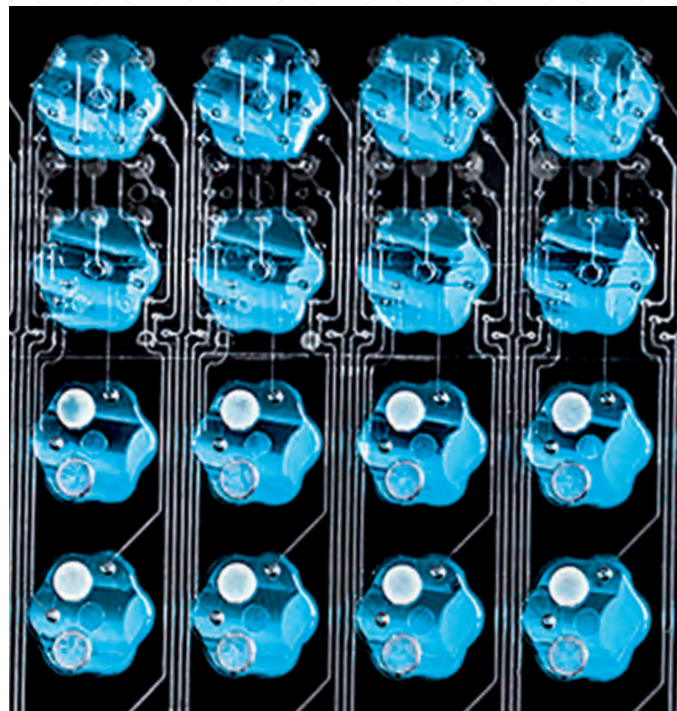
Measurements



E. coli (two triplicates using different P&I settings) WR medium, 37°C, 800 rpm, $pH_{set} = 6.4$, One-sided pH control (NaOH), Feeding rate = 5 μ L/h Glucose (500g/L), Start feed at 5h, Round Well Plate

BioLector® Pro – *E. coli* Fed-batch Fermentation

32 Parallel Microbioreactors



Features

Online Measurement

- Biomass concentration
- pH value
- Dissolved oxygen (DO)
- NAD(P)H and riboflavins
- Fluorescent molecules (GFP, YFP, DsRed ...)
- Temperature
- Humidity
- O₂ in head space atmosphere
- CO₂ in head space atmosphere

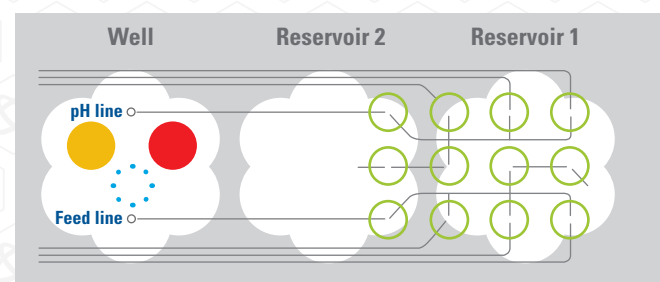
Online Control

- pH value
- Feeding
- Shaking speed
- Temperature
- Humidity
- O₂ in head space atmosphere
- CO₂ in head space atmosphere

System Performance

- Working volume of 800 – 2400 µL
- 32 parallel microreactions
- 16 reservoir wells
- Individual pH control
- Continuous individual feeding
- Broad range of $k_L a$ values (25 – 600 1/h)
- Continuous gas exchange and oxygen supply
- Equal power input to each reactor
- Defined engineering parameters and scalability
- Controlled gas atmosphere (CO₂, O₂ and N₂)
- Feeding modes: constant, linear, exponential or signal triggered

Operating Principle



Dissolved oxygen Biomass & fluorescence pH value Micro-valves

Microfluidic Control on a FlowerPlate® with Optodes

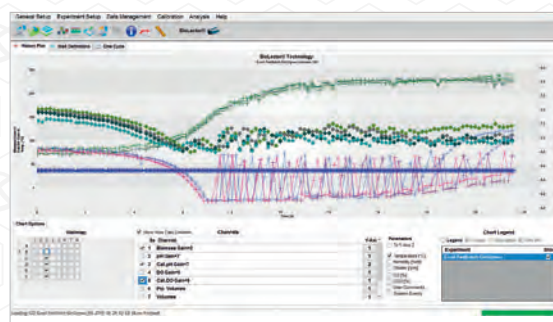
Smaller and Smarter

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Advantages

- Real time kinetics in 32 parallel fermentations
- Microfermentation in standard MTP format
- Batch and fed-batch cultivation
- Control of pH on-the-plate
- Continuous controlled feeding on-the-plate
- DO- and signal-triggered feeding
- High-throughput and easy automation
- Broad linear range for biomass detection (up to 100 g/L CDW, 600 OD)
- Small volume (800 – 2400 µL)
- Excellent reproducibility
- No edge effects
- Continuous shaking operation (no artefacts)
- Defined mass transfer conditions
- Reliable scale up to benchtop fermenters
- Industry leading data analysis software
- Fast and easy data analysis included
- A valuable tool for PAT and QbD

Intelligent Software



Data Analysis with the BioLector Software

Technical Specifications

BioLector® Pro

SYSTEM

| Operation conditions | |
|----------------------|---|
| Plate format | 48 (32 reactor, 16 reservoir wells) |
| Volume | 800 – 2400 µL (depending on microtiter plate) |
| Temperature, minimum | 5 °C below RT (room temperature) |
| Temperature, maximum | 50 °C |
| Gas atmosphere | Only air (optional modules, see below) |
| Humidity | > 75 % rH |
| Orbital shaker | 400 - 1500 rpm at 3 mm (diameter) |
| Feed rate | Two feed lines/well with dosing down to 100 nL, max. 100 µL/h |
| pH control | Over the whole measurement range |

| Modules | |
|--------------------|--|
| Dimensions (W×H×D) | 795 mm × 333 mm × 470 mm 600 mm × 478 mm × 450 mm add. valve control unit |
| Weight | Approx. 40 kg |
| Power source | 100 - 240 V (50/60 Hz) |
| Interface | Ethernet |
| Ambient conditions | 15 - 40 °C, max. 75 % rH |
| Automation | Optionally, the BioLector® can be integrated into the RoboLector® liquid handling systems. |

Art.-No.: G-BLMFL-101

| Optical measurements | |
|---|----------------------------------|
| Filter configuration | up to 6 different filters |
| Preinstalled filters | Biomass, Riboflavin, pH and DO |
| Wavelengths | 365 nm – 800 nm |
| MTP read time | down to 2 min/parameter/32 wells |
| Linear range of cell counts | |
| Microfluidic Plate | (MTP-MF32-xx) 1.0 - 600 OD *1 |
| FlowerPlate® | (MTP-48-xx) 0.2 - 600 OD *1 |
| *1 (0.1 - 100g/L CDW; <i>E. coli</i> , 37 °C, 1000 µL, 800 rpm) | |

| Monitoring / Control | |
|----------------------|---|
| Calibration | Precalibrated plates |
| Measurement range pH | 4.5 - 7.5 depending on plate type in buffered systems |
| Range pH control | 5.5 - 7.5 |
| Measurement range DO | 0 - 100 % oxygen saturation |
| pH control | By acid or/and base |
| Application mode | Disposable technology |

Note: The BioLector® Pro includes the BioLecture software pre-installed on a notebook.

OPTIONAL MODULES

| Art.-No. | Module description | Application | Additional feature | Note |
|--------------|---|---|--|---|
| E-02-25 | O ₂ -downregulation module | Fermentation at O ₂ reduced air, microaerophilic conditions | Control of gas atmosphere: 2 – 21 % O ₂ | |
| E-C02-10 | CO ₂ -upregulation module | Fermentation with CO ₂ controlled gas atmosphere | Control of gas atmosphere: 0 – 10 % CO ₂ | |
| E-AN-200 | BL-Module for anaerobic cultivation | Strict anaerobic fermentation + small, controlled gas flow | Gassing with pure N ₂ or CO ₂ or other defined gases | Operates only with standard 48 well plate |
| E-FRET-100 | BL-Option for FRET measurement (dependent on application) | FRET measurements in BioLector® (1× excitation / 2× emission fluorescences) | Additional measurement of a second, synchronous emission wavelength | Two photodiodes installed |
| E-OP-101-199 | LED/Filter module | Measurement of additional fluorescences in the BioLector® | Measurement at additional wavelengths | Custom made filter modules available |

It is possible to combine all types of modules (O₂, CO₂, FRET) in one device.

ORDERING

Leasing option available

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The Company

m2p-labs is a worldwide leading supplier of microbioreactors.

The company focuses on microreaction and automated solutions for screening and bioprocess development. The microfermentation technology enables customers to conduct experiments with greater efficiency, better quality and lower cost than in any other cultivation platform. More knowledge from small scale leads to more rational and reliable decisions in the development of bioprocesses.



PRODUCT PORTFOLIO

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Systems

The BioLector® microbioreactor is a unique high-throughput fermentation system. In up to 48 parallel cultures the essential fermentation parameters such as biomass concentration, pH and DO as well as fluorescent proteins or substrates can be all monitored online. The advanced BioLector® Pro technology is using proprietary microtiter plates with an integrated microfluidic chip. By using the microfluidic technology the system continuously controls the pH of each culture individually as well as the feeding for fed-batch cultivations. The BioLector® microbioreactors are established systems for bacterial, yeast, fungi, plant and insect cells. All systems are suitable for aerobic, microaerophilic and strict anaerobic cultivations.

Disposables

m2p-labs provides worldwide unique microtiter plates with improved oxygen transfer and excellent mixing properties. Due to its design, the FlowerPlate® supplies microbial cultures even with high oxygen demands with a sufficient amount of oxygen. In addition, the proprietary microfluidic plate uses 16 donor wells for online feeding and pH control. The round well plate delivers moderate oxygen transfer for organisms with lower demand in oxygen or organisms sensitive to shear stress. All plates are available with different optical sensors for different applications.

Automation

The RoboLector® provides an unique automated cultivation platform combining the high-throughput fermentation and the online monitoring capability of the BioLector® with the very accurate and reproducible pipetting of a liquid handling robot. The system is used for media preparations, automated sampling and dosing steps, inductions and fed-batch processing.

www.m2p-labs.com

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