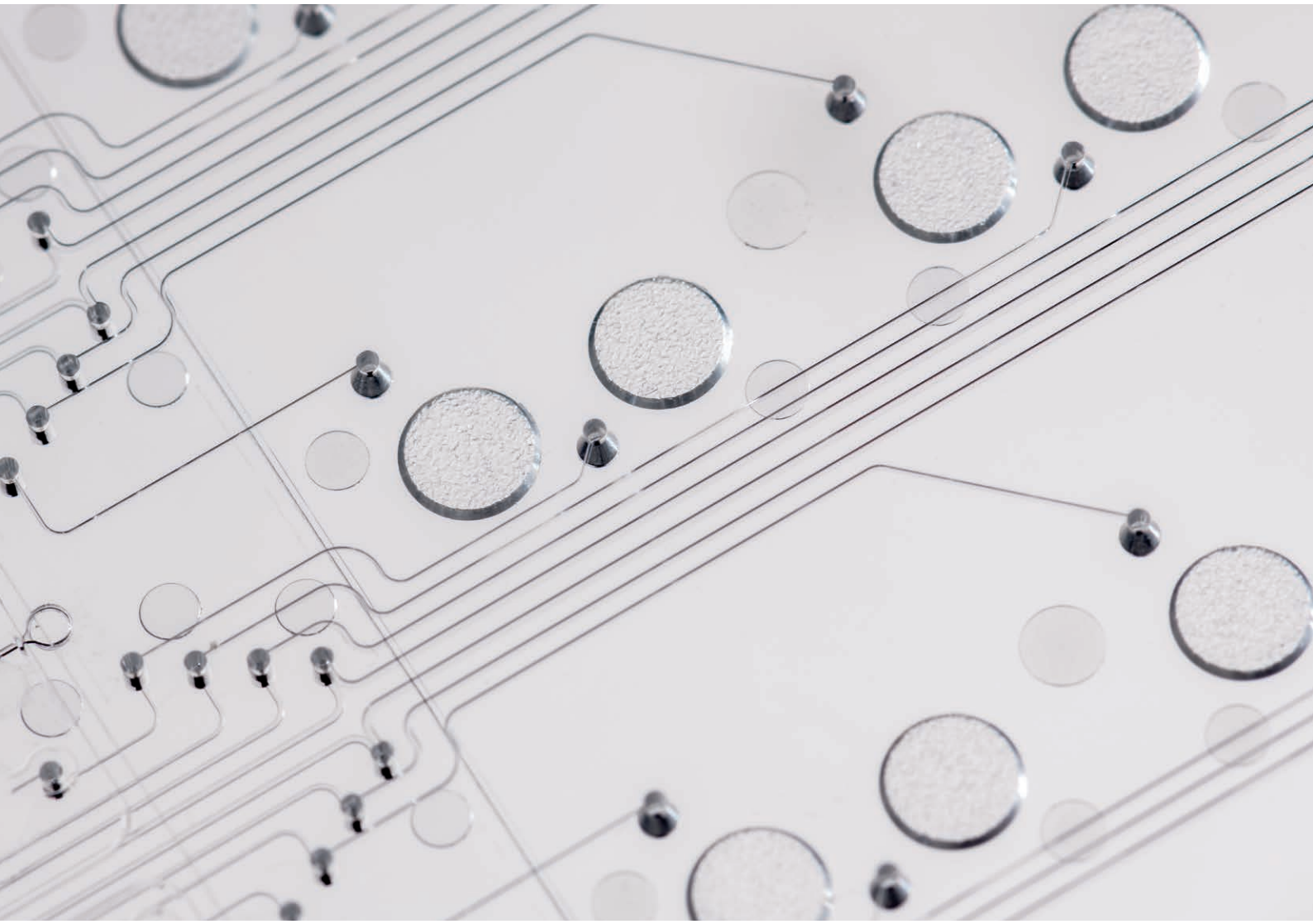
NextGen Microfluidic Microtiter Plate

Flexible BioProcess Control

Continuous Feeding & pH Control
High-Throughput Fermentation
Flower-Shape or Round Well Geometry
Real-Time Monitoring
Scalability



Enhanced Bioprocess Control On-the-Plate
Individually Fed and pH regulated Wells

The NextGen Microfluidic Microtiter Plates facilitate high-throughput screening in up to 32 individually controllable cultivation wells.

The proven technology of microscale feeding combined with non-invasive measurement of the most relevant fermentation parameters, e.g. biomass, as well as pH, DO and fluorescence, enables an industrially-tailored bioprocess development and its optimization. All 32 cultivation wells can be controlled individually through microvalves and microfluidic channels allowing for high-precision pH control and feeding at a CV (coefficient of variation) of < 6% with regards to the pump rate*1. Overcome the limitations of static batch processes and screen within defined conditions for successful upscaling. The beta-irradiated, fully disposable, ready-to-use plate means no tubing and no liquid handling is required.

*1 Determined with a fluorescein-containing buffer at a constant pump rate of 5 µL/h.

Features

Online parameters

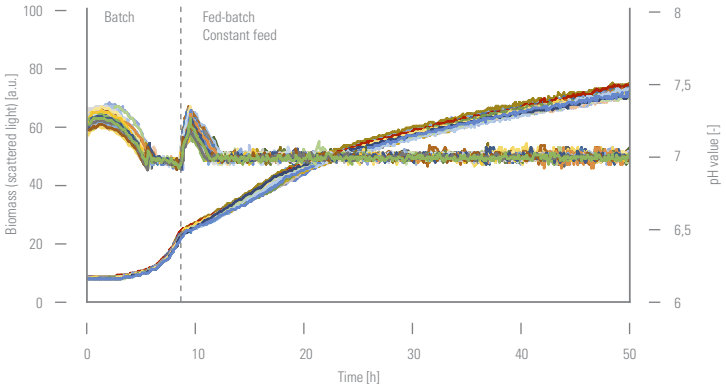
- Biomass
- pH value
- Dissolved oxygen (DO)
- NAD(P)H and riboflavins
- Fluorescent molecules (GFP, YFP, DsRed …)

Applications

- Fed-batch development*2
- pH profiling*2
- Feeding rate optimization*2
- Media screening and optimization
- Fermentation parameter optimization
- Cell line and strain screening
- Statistical design of experiments (DoE)
- Enzyme and cell activity tests
- Inhibition and toxicity tests

*2 Unique characteristic of microfluidic microtiter plates

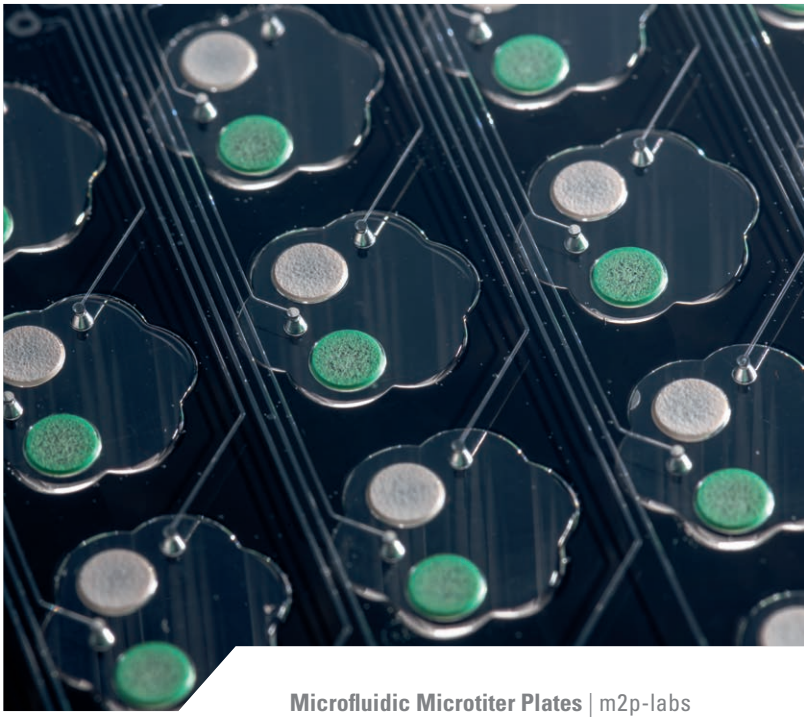
Measurements



E. coli (32-replicate) cultivation in a BioLector® Pro using NextGen Microfluidic FlowerPlate®

Wilms-MOPS mineral medium, 37 °C, 1200 rpm, pH_{set} = 7.0, one-sided pH control (NaOH), feeding rate = 5 µL/h with glycerol (500 g/L), start feed at DO > 70 % (at 8.8 h, after an initial trigger of DO < 60 %)

32 Parallel Microbioreactors



Microfluidic Microtiter Plates | m2p-labs

Features

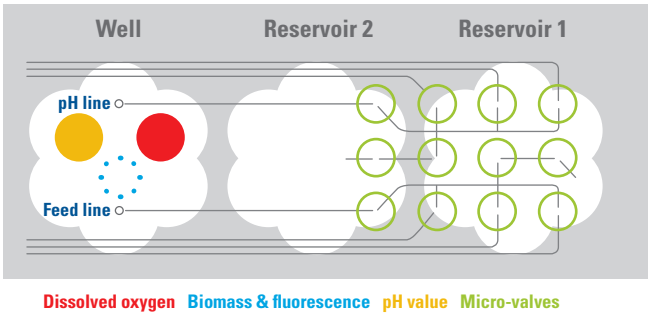
Online Control

- pH value
- Feeding
- Shaking speed
- Temperature
- Humidity
- O_2 in head space atmosphere
- CO_2 in head space atmosphere

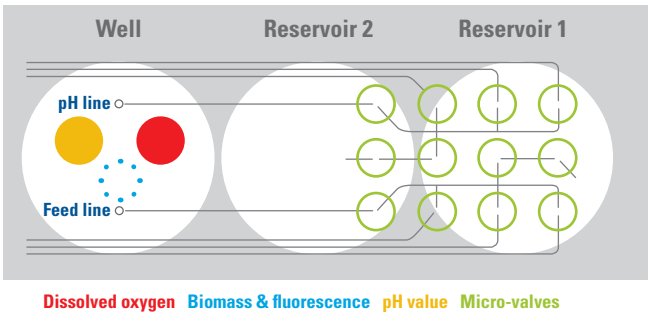
System performance

- Proprietary flower shape or round well geometry
- Working volume of 800 – 2400 µL
- 32 parallel microreactors
- 16 reservoir wells
- Individual pH control (down to pH 4)
- Continuous individual feeding
- Broad range of k_La values (30 – 650 h^{-1})
- Scalability to lab fermenters
- Feeding modes: constant, linear, exponential or signal-triggered

Operating Principle



Microfluidic Control on a FlowerPlate® with Optodes



Microfluidic Control on a Round Well Plate with Optodes

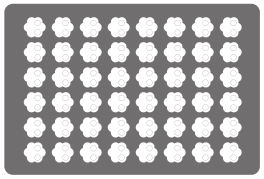
Feeding or pH control - 16 individual solutions

The microfluidic microtiter plates provide the first two well rows as reservoirs for the desired feeding solutions, the remaining 32 wells work as distinct bioreactors. The task for each reservoir row can be chosen independently, either enabling the system to deliver two different feeding solutions, or one feed and one pH value up-/down-regulation, or two-sided, acid and base pH control for each well column. Constant, linear or exponential feeding can be chosen while a closed loop controller ensures proper pH control. Pressurized air actuates membrane valves on the microfluidic chip to pump liquids through independent microchannels to each cultivation well. The complete plate remains a closed system and is a disposable item.

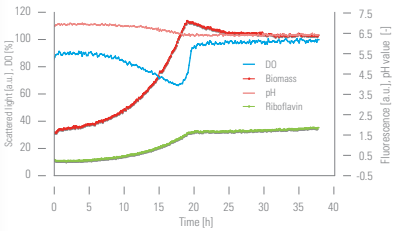
FlowerPlate®

- Multiparameter reading in 32 parallel bioreactors
- Flower shape acts like baffles (suitable for fermentation of bacteria and yeast)
- High mass transfer
  OTR > 0.11 mol/L/h (k_La > 650 h^{-1})
- Wide volume range (800 – 1900 µL)
- Scalability to production fermenters
- No optical cross talk
- Effective mixing

Measurement Principle



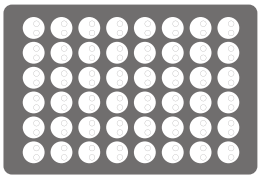
Measurement Example



Round Well Plate

- Multiparameter reading in 32 parallel bioreactors
- Round geometry is suited for shear stress sensitive or filamentous organisms
- Broad range of k_La values (30 – 160 h^{-1})
- Wide volume range (1000 – 2400 µL)
- Scalability to production fermenters
- No optical cross talk
- Effective mixing

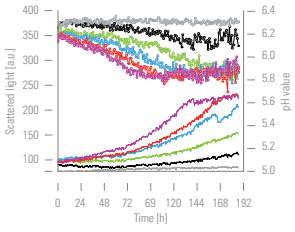
Measurement Principle



Measurement Example

Growth studies with Sf-9 suspension cells with different inoculation cell densities in 48-well Round Well Plate.

- Medium
- 0.5 × 10⁶ cells mL⁻¹
- 0.75 × 10⁶ cells mL⁻¹
- 1.0 × 10⁶ cells mL⁻¹
- 1.25 × 10⁶ cells mL⁻¹
- 1.5 × 10⁶ cells mL⁻¹



Available plate types

MTP-RMF32C-BOH 1	Microfluidic Round Well Plate (48 well format) incl. HP8/Pst3 pH/DO optode/cultivation well
MTP-RMF32C-BOH 2	Microfluidic Round Well Plate (48 well format) incl. LG1/RF pH/DO optode/cultivation well
MTP-RMF32C-BOH 3 (low pH)	Microfluidic Round Well Plate (48 well format) incl. pH51/RF pH/DO optode/cultivation well
BOH 1/ 2/ 3	BOH 1: HP8/Pst3 (ID 402/403) BOH 2: LG1/RF (ID 421/428) BOH 3: pH51/RF (ID 424/428)

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