

Bioreactors

Bioreactor Systems

For Rapid Bioprocess Development



BioXplorer 100

Compact screening with high information content

Based on an 8 reactor block, with a maximum value of 100 ml or 200 ml, the BioXplorer 100 is a high throughput, bioprocess screening system. Designed for working volumes from just ml in blocks of 8 individually controlled bioreactors. Blocks can be combined to give even larger number of parallel reactors.

- | Fully automated, high information content screening tool ideal for DOE studies, with all the typical sensors and controls
- | Most compact system for optimised use of bench space
- | Highly cost effective system for scalable, rapid, high throughput bioprocessing
- | Ideal for cell line/strain screening, media optimisation and small scale process development
- | Suitable for robotic integration

Typical BioXplorer 100 configuration



8 parallel reactors totally independent in temperature, stirring and all other process conditions. Multiple blocks can be combined

Block for the 100 range reactors



8 reactor block can also fit on liquid handling robots for automated sampling and downstream processing

Bioreactors compatible with the BioXplorer 100 System



| | | | |
|---------------------------|----------------|-----------------|-----------------|
| Bioreactor Volumes | 100 ml | 200 ml | 200 ml |
| Working Volumes | 20 ml to 70 ml | 20 ml to 150 ml | 20 ml to 150 ml |

BioXplorer 400

Flexible, high data content optimisation

Based on a 4 reactor block, the BioXplorer 400 provides the ideal platform for bioprocess development and optimisation using 4 or 8 reactors in parallel with fermentation working volumes up to 400 ml.

- | Most versatile bioprocessing platform for development and optimisation
- | High information content and excellent scalability to large scale bioreactors
- | Reduce media costs and optimise the use of bench space

Block for the 400 range reactors



Typical BioXplorer 400 configuration



8 parallel reactors (using 2 blocks) totally independent in temperature, stirring and all other process conditions

Four different size reactors interchangeable on the same reactor block. Multiple blocks can be combined

Bioreactors compatible with the BioXplorer 400 System



| | | | | | |
|---------------------------|----------------|-----------------|-----------------|-----------------|-----------------|
| Bioreactor Volumes | 100 ml | 200 ml | 500 ml | 200 ml | 500 ml |
| Working Volumes | 20 ml to 70 ml | 20 ml to 150 ml | 60 ml to 400 ml | 20 ml to 150 ml | 60 ml to 400 ml |

Elevated Press

BioXplorer 100P - 400P

**Parallel high pressure mini bioreactors
200 ml to 1 L systems**



4 x 500 ml high functionality reactors rated to 10 bar, on a linear (AutoMATE) platform. Simpler reactor configurations can be fitted on compact reactor blocks

Bioreactors compatible with the BioXplorer 100P - 400P System



| | | | |
|---------------------------|-----------------|-----------------|-----------------|
| Bioreactor Volumes | 200 ml | 500 ml | 1000 ml |
| Working Volumes | 20 ml to 150 ml | 60 ml to 400 ml | 60 ml to 700 ml |

BioXplorer 5000P

Designs for larger 1 to 20 L systems

- | Floor standing frame
- | Easy bioreactor manipulation
- | Built in Steam in Place (SIP) operation



Easy to open top and change internals



Range of interchangeable reactors available up to 20 L



2 L Bioreactor rated to 10 bar with SIP, with custom configurations

ure BioXplorer

Benefits Of Pressure

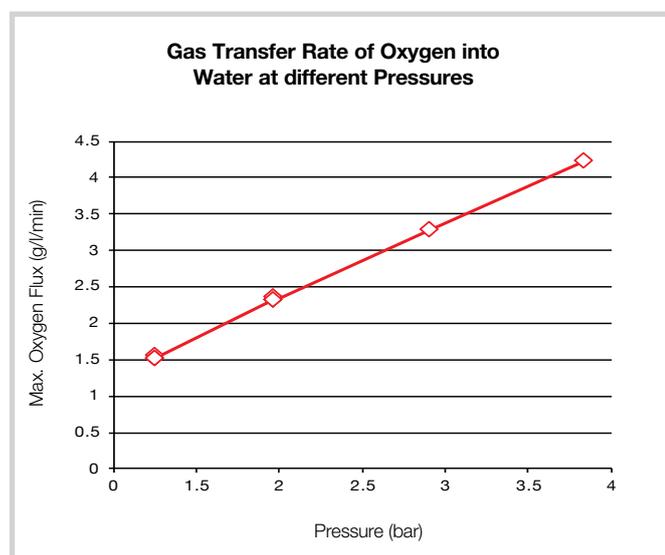
Elevated gas pressure increases the solubility of gases and can produce commercial benefits in both bacterial and cell culture applications.

The BioXplorer P range can operate up to 10 bar providing benefits which include:

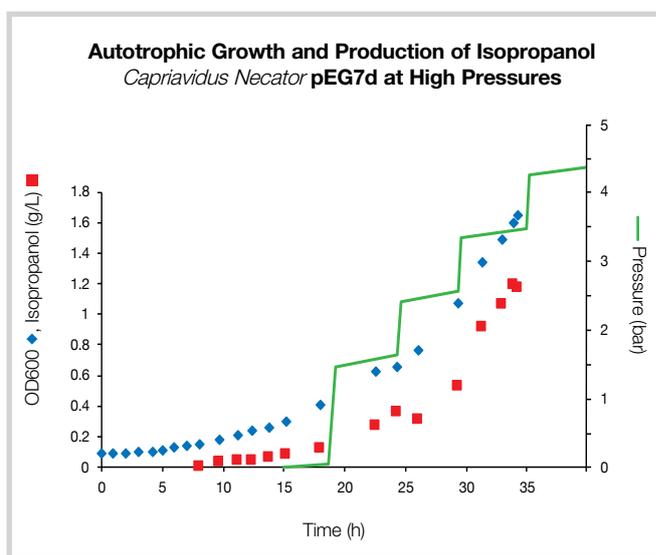
- | Increased gas fermentation rate
- | Enhanced gas transfer rate (beyond high KLa limits)
- | Replication of pressure effects of large scale operations
- | Reduced dependence on sparging/agitation for gas availability

Highly controlled pressure regulation and monitoring in each reactor is provided additional to normal controls such as DO, pH, OD, liquid dosing etc.

A range of features dealing with operator safety are included as standard.



500 ml reactor stirred at 1500 rpm, as pressure is increased in steps from 1 bar to 4 bar



Growth was sustained during the whole cultivation. Specific rate of isopropanol was maintained at a high level to the end. Experiments in 500 ml stirred bioreactors with control and monitoring of pH, DO and optical density. (REF: Guillouet, LISPB, France, 2018)

Key Features P Range

- | Independently controlled single or multiple parallel bioreactors
- | Range of stainless steel pressure vessels available, rated up to 10 bar (145 psi) with working volumes starting from 20 ml
- | Automated pressure monitoring and control of each bioreactor
- | Highly instrumented bioreactors with pressure rated probes, feeds and filters
- | Option of complex automated gas feed strategies with feedback to off gas analysis systems allowing real time response to changes in head-space gas composition
- | Elevated pressure sampling system for convenient sampling throughout the process
- | System capable of temperatures from ambient to 225 °C allowing higher temperature applications, Steam in Place (SIP) option and downstream processing normally requiring a dedicated chemical process development system
- | Full suite of safety features

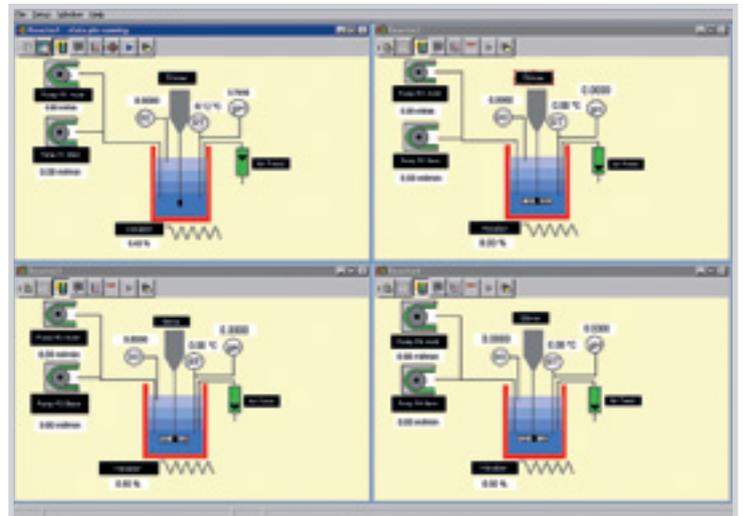
BioXplorer Accessories

Compact screening with high information content

Software Control

Class leading powerful software with a range of add on modules. All BioXplorer parameters can be monitored/controlled including:

- | Temperature
- | Gas feeds, flow and mix
- | pH
- | Dissolved oxygen
- | Redox
- | Stirrer speed
- | Torque (for viscosity indication)
- | Pressure
- | Liquid feed rates
- | Antifoam and level detection



Gas Feeds

- | Choose from simple or more sophisticated gas flow control regimes
- | Each bioreactor can be configured with single or multiple mass flow controllers
- | For microbial fermentations, automatic oxygen enrichment is possible if an air and oxygen (or enriched oxygen) source is supplied – the controller can be set to maintain a chosen dissolved oxygen (DO) value by altering the amount of supplied gas
- | For cell culture applications CO₂ can be used for pH control
- | Ratios of several gases can be mixed and regulated with online feedback from off gas analytics



Liquid Feeds

- | Choice of liquid feeds for standard and pressure applications
- | Highly linear peristaltic pump drives are integrated into standard heads which enable exceptional pH and dosing control as well as a wide operating range
- | Typically, two to four pumps per reactor are supplied but additional pumps can be added as needed
- | Syringe pumps and high pressure pumps are also available



Magnetically Suspended Stirring

- | HEL's proprietary design is recommended for reactors up to 500 ml
- | Ideally suited to small bioreactors with proven performance
- | No shaft seal or moving parts: no sterility issues
- | Excellent magnetic coupling
- | Range of stirrer designs (marine, rushton, etc)
- | Speed 300 rpm to 1500 rpm or 30 rpm to 200 rpm



Overhead Stirring

- | Overhead stirring is offered on vessels from 300 ml upwards and is commonly used for larger bench-scale reactors
- | For pressure applications special magnetic drives are used



pH, Dissolved Oxygen and Redox

A complete range of bioprocess probes are available to cater for different conditions, reactor sizes and applications. All probes are integrated into software to allow automated monitoring and feedback loops.



Off Gas Analysis

Tandem off-gas analysis units as an on-line tool to monitor and control a process continuously. By monitoring the off-gas, the software can automatically calculate the oxygen uptake rate (OUR) of the cultivated cells and the carbon dioxide production rate (CPR) can be measured for micro-organisms. From this data, the respiration quotient (RQ) can be calculated automatically.



Cell Density and Biomass Monitoring

BioVIS allows the online monitoring of cell growth and biomass using optical density, which can reduce or replace the need for online sampling. This feature allows the user to track the growth and understand the processes without taking samples. Viable cell density probes can also be integrated.



Robot Integration

Robotic sampling and work-up as required.



Specifications

| | BioXplorer 100 / P | BioXplorer 400 / P | BioXplorer 5000P |
|-----------------------------|---|---|---|
| Parallel Bioreactors | 8 or more | 4 or more | 2 or more |
| Vessels | Glass Stainless Steel | Glass Stainless Steel | Glass Stainless Steel |
| Working Volumes | 20 ml to 150 ml | 20 ml to 150 ml 60 ml to 700 ml | 20 ml to 15 L |
| Stirring Speed | 250 rpm to 1500 rpm* | 250 rpm to 1500 rpm* | 50 rpm to 1500 rpm* |
| Impellers | Rushton Marine Pitched | Rushton Marine Pitched | Rushton Marine Pitched |
| Stirring Drive | Magnetic drive | Magnetic drive Overhead drive | Overhead drive |
| Temp. Range | -20 °C to 200 °C** | -20 °C to 200 °C** | -20 °C to 225 °C** |
| Temp. Control | Integrated, individual electrical heating in the block, software controlled | Integrated, individual electrical heating in the block, software controlled | Heated jacket Circulator |
| Applications | Mammalian Microbial Gas Fermentation | Mammalian Microbial Gas Fermentation | Mammalian Microbial Gas Fermentation |
| pH Control | Acid/base liquid feed; Gas addition | Acid/base liquid feed; Gas addition | Acid/base liquid feed |
| Liquid Feeds | Optional anti-foam; substrate feeds | Optional anti-foam; substrate feeds | Optional anti-foam; substrate feeds |
| OD Measurement | Optional | Optional | Optional |
| Gas Mixing | Air, H ₂ , N ₂ , O ₂ , CO, CH ₄ and CO ₂ | Air, H ₂ , N ₂ , O ₂ , CO, CH ₄ and CO ₂ | Air, H ₂ , N ₂ , O ₂ , CO, CH ₄ and CO ₂ |
| Max Pressure | Up to 10 bar with stainless steel vessels | Up to 10 bar with stainless steel vessels | Atmospheric - 10 bar |

*Speeds depend on stirrer drive, media properties and aeration rate.

**Sub-ambient cooling requires optional cooling module.

About HEL

HEL is an international company that specialises in chemical reactors, bioreactors and related data/logging tools for process R&D in the pharmaceutical, fine chemical, biotechnology and petrochemical industries. Established in 1987 and with clients worldwide our key strengths are:

Knowledgeable staff - highly qualified and experienced chemical engineers and chemists

Quality - underpinned by ISO9001 certification for over 16 years

Service - choice of service contracts backed by an established culture of unmatched client support

Range of products - both off-the-shelf and custom designs, manual and fully automated controls, low and high pressure/temperature applications, single and parallel/multi-vessel products

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