

FLUOROMETRIX

empowerment through enlightenment

Cellstation™

High Throughput Bioreactors

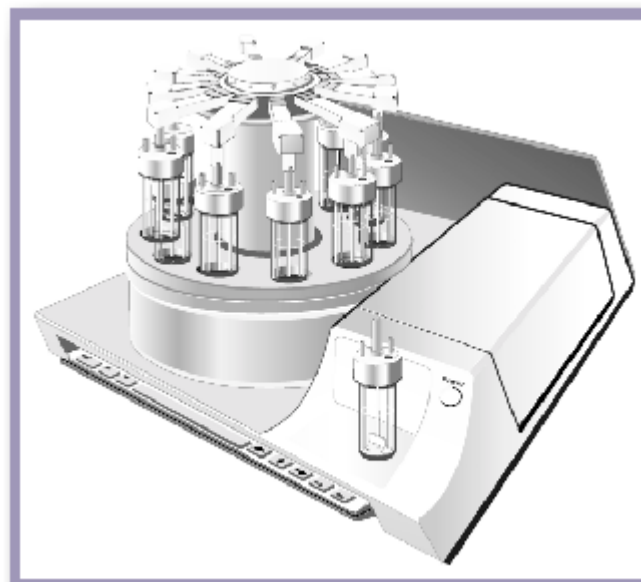
Enables highly parallel bioprocessing by a multiple-vessel architecture with non-invasive monitoring and optional control of critical process parameters.

Cellphase®

Non-invasive Sensors *pH, DO, pCO₂*

Enables non-invasive optical measurement of critical bioprocess parameters: pH, DO and pCO₂.

*Increasing Yield Through
Non-invasive Measurement &
Control*



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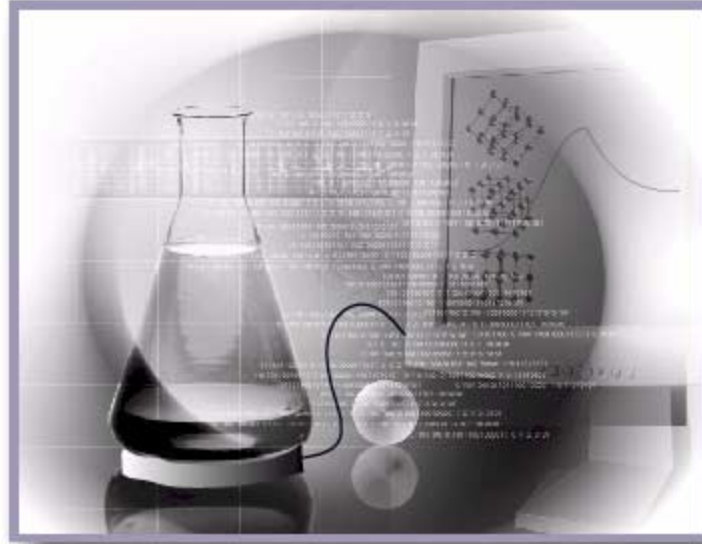
Cellphase®

Non-invasive Sensors

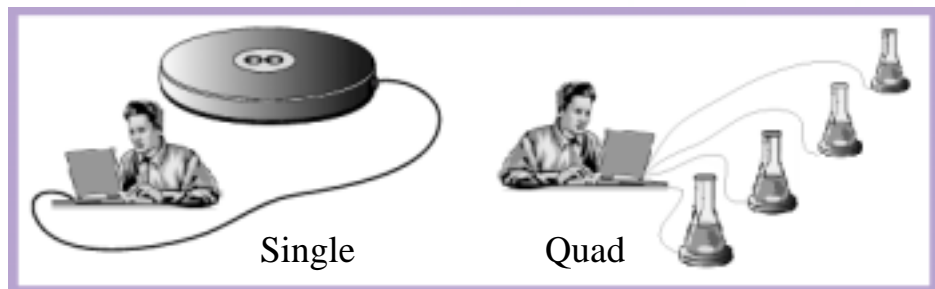
pH, DO, pCO₂

Cells are profoundly affected by their environment. DO (dissolved oxygen), pH, pCO₂ (dissolved CO₂) and temperature are critical to their growth and product formation characteristics. Naturally, in a bioprocess, one must control the above parameters at an optimal level. However, the conventional sensor technology needed to do so is decades old, cumbersome and expensive such that it is applied only to larger scale systems. The vast majority of cultivations are done "blind" where cells are placed in a vessel (shake, spinner, T-flasks, etc..) containing a nutrient solution and placed in a temperature controlled environment and allowed to grow unmonitored and unregulated.

Fluorometrix has a paradigm shifting approach that relies on simple peel-and-stick sensor patches that are introduced into any transparent vessel and non-invasively monitored optically from outside the vessel. These patches are disposable and can be manufactured as an integrated part of the vessel. Cellphase® was engineered to be a low-cost non-invasive sensor. It is now in use in most of the major pharma/biotech companies and has served to validate the need for such technology.



Fluorometrix Corporation offers a full line of disposable non-invasive optical sensor instruments for measuring pH, DO and pCO₂. Our "coaster" design, using inexpensive, sterilizable "peel-and-stick" foils, affords ease-of use with virtually any vessel providing a clear optical path - flasks, reactors, bags.



Configuration package available in quad (four multiplexed sensors) or single packages. Interface to PC is through standard USB port.

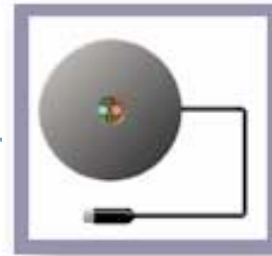
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Cellphase®

Non-invasive Sensors

pH, DO, pCO₂



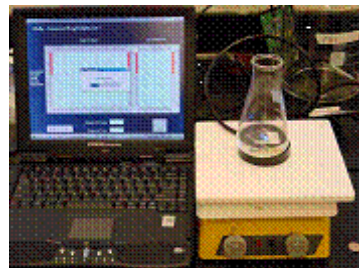
Finally, you can non-invasively gain access to online data for precision monitoring and control of your fermentation and cell culture experiments.

Specifications

- DO range: 0-100% air nominal
- pH range: 5.5-8.5 nominal
- pCO₂ range: 0-25% nominal
- Sensing platform 3" diameter
- 3, 8 or 12 foot cord to PC
- Standard USB PC interface
- Draws power from USB
- Software included
- Warranty: 90 days

Key Features

- Non-invasive
- Compact
- Easy to use design
- Ideal for laboratory use
- Real-time and continuous
- DO to 100% air
- High accuracy at low DO
- USB interface
- ideal for unattended operation



Cellphase® Sensing System



Flask and Patch

Custom solutions available on request. OEM adaptations to existing bioprocess systems available under extended terms and/or sublicensing core technology.

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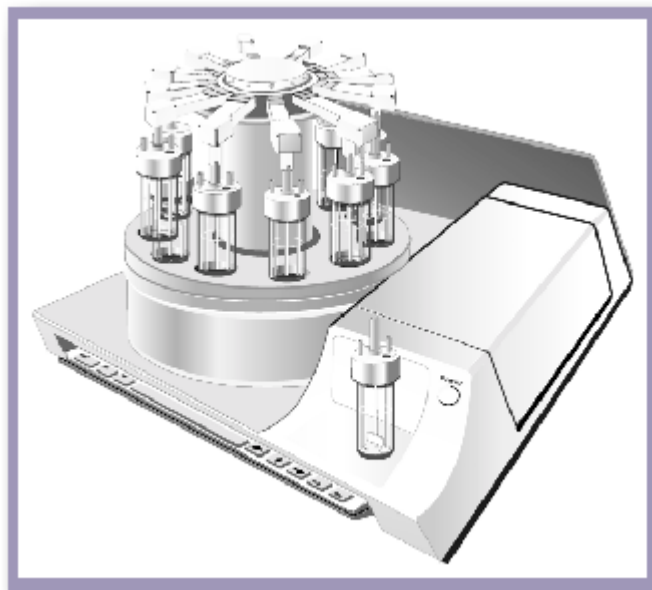
Key to the design of Cellphase® is the non-invasive nature of the system. Unlike most existing sensors requiring the physical insertion of a probe into the fluid to measure dissolved oxygen, Cellphase® actually resides outside the fluid, illuminating a special chemically treated luminescent patch residing within the fluid with light energy. This causes, in response, a luminescent light energy to be generated which, when collected and properly analyzed, provides precise information on the concentration of dissolved oxygen in the fluid. This non-invasive technique helps prevent contamination of the fluid being tested, thereby providing a means for monitoring and controlling chemical reactions in a closed vessel without contaminating or stopping the bioprocess being analyzed.

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Cellstation™

High Throughput Bioreactors

The Cellstation™ family of products are designed to enormously expedite both the discovery and process development stages of fermentation and cell-culture based products. The Cellstation™ presents a viable and cost-effective compromise between the parallelism of shake flask culturing and the monitoring and control capabilities of culturing with a lab-scale bioreactor. The cost savings resulting from the use of the Cellstation™ system result directly from its ability to increase yield in the bioprocess laboratory and lead to productivity increases at far lower cost compared to the competition.



Fluorometrix Corporation introduces the Cellstation™ family of High Throughput Bioreactors (HTBR™), with non-invasive sensing and optional control of critical bioprocess parameters in a multi-reactor, multi-sensor architecture: pH, DO (dissolved oxygen), OD (optical density) and Temperature.



Cellstation™ systems protected by US and international patents.

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Cellstation™

High Throughput Bioreactors

The Cellstation™ product family, which involves the sensing and control of bioprocess parameters in a multi-reactor system, is designed to enormously expedite both the discovery and process development stages of fermentation and cell-culture based products. The Cellstation™ family leverages the Company's patents for multiple non-invasive sensor platforms and will be brought to market with a variety of features at a variety of price points. Fluorometrix' initial entry into the market place, the Cellstation™, is shown in the picture to the right.

The core technology in Cellstation™ is based on the Cellphase® non-invasive sensing system.



Key advantages are deployment of pre-calibrated, disposable bioreactors that confer enormous time and labor advantages over traditional technology.

Specifications

- 12 mini stirred tank reactors
- Vessel volumes: up to 35 ml*
- Measures pH, DO, OD
- pH range: 5.5-8.5 nominal
- DO range: 0-100% air nominal
- Temperature control optional
- Individual agitation rates
- Agitation rates: 10-1000 RPM
- Integrated PC (Monitor optional)
- Autoclavable reactors
- Dimensions (in): 24x21x18**
- Power: 120VAC (220 optional)
- Weight: ~50 pounds
- Warranty: 1 year

*Vessel working volumes

**Nominal depending on selected options

Key Features

- Rotary drive
- Sequential monitoring
- Simple set-up / breakdown
- Simple & rapid calibration
- Compact bench-top design
- Single sampling platform
- Non-invasive measurement
- Compact
- Ideal for laboratory use
- Real-time and continuous
- DO to 100% air
- High accuracy at low DO
- Disposable glass vessels

Cellstation™ available in a variety of configurations complete with standard option selections. Custom configurations available on request – please call.

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Cellstation™

High Throughput Bioreactors

The single major bottleneck in biologics development is the ability to grow cells in monitored & controlled environments. pH, oxygen and nutrients affect cell product formation. Clearly, cells grown under optimal conditions produce more product. With a vast number of combinations possible, the key limitation is sensor technology – until now.

The Cellstation™ presents a viable and cost-effective compromise between the parallelism of shake flask culturing and the monitoring and control capabilities of culturing with a lab-scale bioreactor.

The system is designed to minimize set-up times and to operate with a minimum of operator intervention, thereby dramatically increasing the productivity of the laboratory scientist.

**Bottom line:
Better, Cheaper, Faster**



Mini Stirred-Tank Platform

Cellstation™ Cost Savings

The Cellstation™ system's ability to decrease time, material and labor in research, process development and production applications leads to lower operating costs and a faster return on investment:

1. Highly parallel system – large numbers of cultures can be run simultaneously
2. Pre-calibrated sensors lead to minimal labor and provide advanced process information
3. The small working volumes result in reduced usage of nutrients and medium
4. Using disposable materials greatly saves labor and reduces contamination
5. Maintenance, calibration and cleaning validation costs are virtually zero

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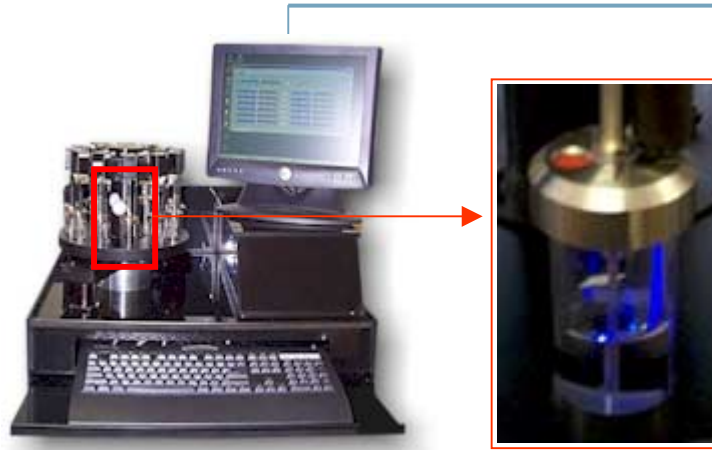
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Cellstation™

High Throughput Bioreactors

While there are a variety of bioreactors on the market today, they rely on invasive measurement techniques to monitor critical process parameters. As a result, they are bulky, and require substantial set-up time. In addition, an added expense for the existing bioreactor segment is the replacement of sensors – a costly and time consuming process. Current bioreactors also require significant break-down time, cleaning and maintenance. The resultant labor burden is a very well known problem to all practitioners in the biotech arena today.

Through the use of non-invasive sensing techniques, multiple well platform architecture and the heavy reliance on low cost disposables, the Cellstation™ enables highly parallel bioprocessing that yields an order of magnitude increase in performance over competing processes/products, at greatly reduced cost both in terms of initial product cost and associated labor costs.



Individual Mini Stirred-Tank

Cellstation™ Design Advantages

1. Rotary device permits sequential monitoring of twelve mini stirred-tank bioreactors (up to 35 ml working volume)
2. Allows for non-invasive, on-line monitoring of pH, DO (dissolved oxygen) and OD (optical density) using fluorescence-based measurement techniques
3. Allows system-wide temperature control using optional water bath
4. Allows for the individual control of agitation rate within each mini stirred-tank bioreactor (10-1000 RPM)
5. Single, multiplexed sensor station ensures consistency of readings
6. Effectively calibration free!

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CellPhase[®]

Example of CellPhase[®] Core Sensing Technology

Theory of Operation

Measuring Fluorescence Lifetime

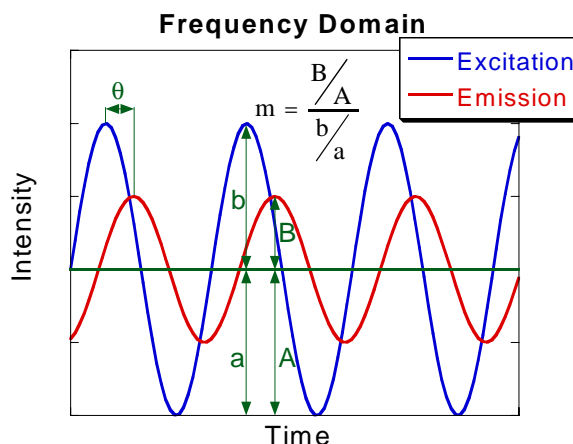
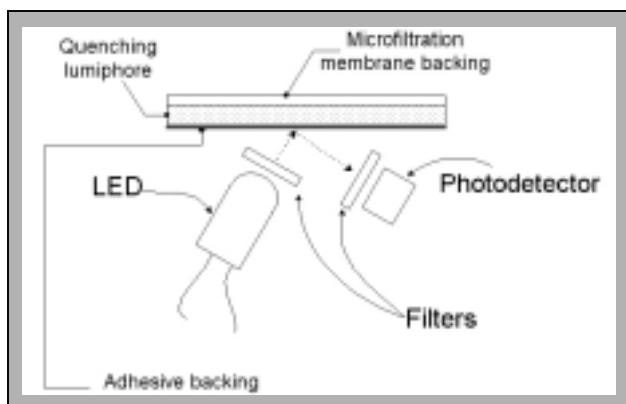


CellPhase[®], the Fluorometrix proprietary sensing technology combines luminescent lifetime chemistry with novel, low cost instrumentation designed to provide effectively non-invasive chemical sensing. This technology significantly outperforms other common types of chemical sensing technologies by minimizing drift, signal degradation and other shortcomings, at a significantly reduced cost in a system that is effectively non-invasive in operation.

Each Fluorometrix system employs a proprietary robust low cost phase-based fluorometer for the real-time monitoring and control of various chemical parameters, housed in a portable package adaptable for retrofit use with existing glassware and other laboratory apparatus, the Fluorometrix Cellstation[™] High Through Bioprocessors family of products included.

Key to the design is the effectively non-invasive nature of the systems. Unlike most existing sensors requiring the physical insertion of an instrument-connected probe into the fluid to measure chemical concentrations, the CellPhase[®] instruments reside outside the fluid, illuminating specially treated luminescent patch(es) residing within the fluid with light energy. This causes, in response, luminescent light energy to be generated which, when collected and properly analyzed, provides precise information on the concentration of select elements, compounds and conditions in the fluid. This non-invasive technique helps prevent contamination of the fluid being tested, thereby providing a means for monitoring and controlling chemical reactions in a closed vessel without contaminating or stopping the bioprocess being analyzed. It also allows a single CellPhase[®] instrument to be used for measuring parameters in multiple vessels, since the sensing instrument itself never contacts the process fluid.

The theory of operation differs for pH, OD and pCO₂ (see selected scientific references on next page).



Purchasing

The Cellphase® and Cellstation™ family of non-invasive sensors and high throughput bioreactors are available direct through Fluorometrix or through select distributors depending on your geographic location. Reference price ranges are shown below but may vary depending on volume and actual configuration. Custom pricing is also available to meet your individual needs. Please call or email us to discuss your individual needs and purchasing options.

Partial Customer List

Millenium
Martek *
Diversa *
Bayer *
Merck *
Advanced Instruments *
Broadley-James
Biomarin *
Tanox
CP Kelco
Exelixis
Glaxo *
Springborn
Sylvan
Schering Plough
Bristol Myers
U. Nottingham*
Genentech *
Hiroyuki
VWR *
Dupont *
Baxter *
Human Genome*
MIT*
Aventis*

*repeat customers

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Worldwide Sales:
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sales@fluorometrix.com

New England Only:
(401) 683-0933
dfrost@qicsontheweb.com

System Description	Reference Price Range (US)
Cellphase® pH Instrument	\$1,950/single, \$5,600/quad
Cellphase® DO Instrument	\$1,950/single, \$5,600/quad
Cellphase® pCO ₂ Instrument	\$1,950/single, \$5,600/quad
Cellphase® Sensing Patches (12 pack)	\$100-\$140
Cellstation™ Reactor Vessels (12 pack)	\$300-\$500
Cellstation™ HTBR-1	\$50k-\$125k (depending on options)
Cellstation™ custom solutions	Please call

Attractive leasing programs available. Please call for details.

Select Scientific References

1. Peter Harms, Yordan Kostov and Govind Rao, Bioprocess monitoring, Current Opinion in Biotechnology 2002, 13:124-127.
2. Haley R. Kermis, Yordan Kostov, Peter Harms, and Govind Rao, Dual Excitation Ratiometric Fluorescent pH Sensor for Noninvasive Bioprocess Monitoring: Development and Application, Biotechnol. Prog. 2002, 18, 1047-1053.
3. Yordan Kostov, Peter Harms, Lisa Randers-Eichhorn, Govind Rao, Low-Cost Microbioreactor for High-Throughput Bioprocessing, Biotechnology and Bioengineering, VOL. 72, NO. 3, February 5, 2001.
4. Xudong Ge, Yordan Kostov, Govind Rao, High-stability non-invasive autoclavable naked optical CO₂ sensor, Biosensors and Bioelectronics 18 (2003) 857/865.
5. **Atul Gupta, Govind Rao, A Study of Oxygen Transfer in Shake Flasks Using a Non-Invasive Oxygen Sensor**, Biotechnology and Bioengineering, VOL. 84, NO.3, November 5, 2003.

Call for additional information (978) 461-2468

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