BioProfile FLEX
The Power of One
Specifications

Sample Analysis Time .....2.5 minutes (Gases only)
4.0 minutes (Chemistry/Gas & Osmolality)
6.25 minutes (All 15 tests)
Operating Temperature Range .....15-30°C (59-86°F)
Operating Relative Humidity Range 20-85%
Sample Size .....1mL (for all modules)
Sampling Options.....Individual via syringe/cup
Automated batch using 20-position sampling tray
On-line, automated from up to ten bioreactors
Host Computer Operating System .....Windows XP
Electrical Requirements .....90-264 VAC, 50 to 60 Hz (Universal Power Supply)
System Size: Height: 20 in (50 cm), Width: 26 in (66 cm), Depth: 20 in (50 cm)
System Weight: Analyzer: 94 lbs (42.6 kg) without reagents
Host Computer Monitor Weight/CPU: 41.5 lbs (18.8 kg)
Safety Certifications: TUV, IEC 61010-1:2001, Quality Systems Certification: TUV: ISO 9001:2000
FDA Registered, OPC Compliant, PAT Compatible, 21 CFR Part 11 Compliant

On-Line Autosampler

Switching Pumping Module
Height: 8.86 inches (22.5cm), Width: 27.4 inches (69.5cm)
Depth:19.4 inches (49.3cm), Weight: 35 lbs (16 kg)
Electrical requirements .....110/230 VoltAC, 50/60 Hz
Automated sampling from up to 10 bioreactors

Reactor Valve Module (RVM)
Height.....7.5 inches (19.5cm)
Width.....4 inches (10.16cm)
Depth.....5.75 inches (14.6cm)
Weight .....4 lbs (2 kg)
Electrical requirements .....Supplied by Switching Pumping Module
Requires one RVM per bioreactor

Sample Retain Collection System (SRCS)
SRCS Sample Rack Capacity.....2 racks
Sample Rack Loading: 15 mL conical centrifuge tubes, 34 tubes per Sample Rack (68 total), 50 mL conical centrifuge tubes, 10 tubes per Sample Rack (20 total)
Retained Sample Volume User Selectable.....0.1 to 50 mL.
Temperature Control: Mode of Cooling .....Thermo electric cold plate
Temperature Range.....3 to 30 degrees centigrade
Dimensions (height x width x depth).....25.3 x 20.7 x 22.2 inches
64.1 x 52.6 x 56.4 centimeters

Chemistry/Gas Module

Assay	Measurement Range	Resolution	Method
Glucose	0.2–30.0 g/L*	0.01g/L	Biosensor
Lactate	0.2–10.0 g/L*	0.01 g/L	Biosensor
Glutamine	0.2–12.0 mmol/L*	0.01 mmol/L	Biosensor
Glutamate	0.2–12.0 mmol/L*	0.01 mmol/L	Biosensor
Ammonium	0.2–25.0 mmol/L	0.01 mmol/L	Direct ISE
pH	5.000–8.000	0.001	Direct ISE
PCO_2	3.0–300.0 mmHg	0.1 mmHg	Direct ISE
PO_2	3.0–800.0 mmHg	0.1 mmHg	Clarke Electrode
Sodium	40–220 mmol/L	0.1 mmol/L	Direct ISE
Potassium	1.0–100.0 mmol/L	0.01 mmol/L	Direct ISE
Calcium	0.10–10.0 mmol/L	0.01 mmol/L	Direct ISE

Calculated Tests: O_2 Saturation; CO_2 Saturation; Temp. Corrected pH, PCO_2, PO_2

**Ranges Reflect User Selectable 1:2 Dilution*

Osmolality Module

Assay	Measurement Range	Resolution	Method
Osmolality	0–1500 mOsm/kg	1 mOsm/kg	Freezing Point

Cell Density/Viability Module

Assay	Measurement Range	Resolution	Method
Diameter	8 – 50 µm	N/A	Digital Imaging
Density	50,000 – 100,000,000 cells/mL	N/A	Digital Imaging
Viability	0 – 100%	N/A	Digital Imaging

IgG Module
Measurement Range: 0.10–10 g/L

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BioProfile® FLEX
The Power of One

Automated Analyzer for Fast Comprehensive Cell Culture Analysis

Custom Test Menus with up to 15 assays

Gluc	Lac	Gln	Glu	NH_4^+	pH	PO_2	PCO_2	Na^+	K^+	Ca^{++}	CD	CV	Osm	IgG

Modular Test Menu Choices
Chemistries/Gases
Cell Density/Viability
Osmolality
IgG

System Integration Options
On-Line Autosampler
Sample Retain Collection System
OPC Connectivity

Automated, Modular, Multi-Test Analyzer for Fast Comprehensive Cell Culture Analysis

BioProfile FLEX is a chemistry/cell viability modular instrument that measures up to 15 key cell culture attributes related to product yield and quality. By combining as many as five separate instruments into one easy-to-use instrument, BioProfile FLEX simplifies workflow and saves time, labor, and operating cost versus multiple instruments.

One Fast, 2-8 Minute Analysis
Saves as much as 30 minutes per sample compared to using multiple instruments.

One Integrated Data Report
Simplifies data collection, analysis, archiving, and regulatory compliance.

One Intuitive, User Interface
Saves 30 or more operator steps compared to multiple instrument interfaces.

One Small, 1 mL Sample
Conserves cell culture mass and end product.

One Consolidated Workstation
The compact BioProfile FLEX footprint saves up to 15-20 square feet of valuable bench space and saves hours of maintenance each month and compared to multiple instruments.

Modular System Field-Upgradable

The modular design of BioProfile FLEX can be customized with one to four analytical modules, to consolidate up to 15 vital cell culture tests. Each module incorporates state-of-the-art measuring technology.

Chemistry and Gas Module
by Electrochemistry

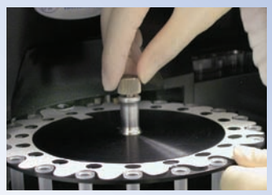
Glucose
Glutamine
Ammonium
PO_2
Sodium
Ionized Calcium
Lactate
Glutamate
pH
PCO_2
Potassium

Cell Density and Cell Viability Module
by Digital Imaging

Cell Density
Cell Viability
Cell Diameter

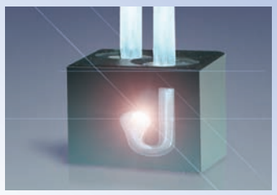
Osmometer Module
by Freezing Point Depression

Osmolality



IgG Module
by Photometry

IgG



Cell Density, Cell Viability Module
by High Resolution Digital Optics

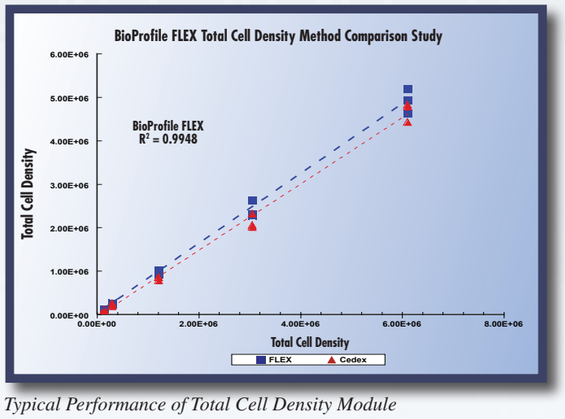
Cell density and cell viability are measured by automated hemocytometry using the trypan blue exclusion assay, combined with high resolution digital optics, and advanced software algorithms. Non-viable cells take up the trypan blue stain and are differentiated from viable cells. Proprietary software algorithms inspect up to 40 high resolution digital images and identify viable (unstained) and non-viable (stained) cells using multiple, selectable image inspection criteria. Cell counting accuracy and precision are enhanced in several ways:

Wide Dynamic Range
A wide dynamic range of cell densities from 50,000 to 10,000,000 cells/mL can be counted in normal operation. The counting range can be extended to 100,000,000 cells/mL by using the 1:10 auto-dilution mode.

Counts up to 40 Optical Fields
BioProfile FLEX counts 40 images, which is 30 times the quantity of cells typically counted by manual cytometry. Accuracy and validity of the cell count is greatly improved using additional counts.

Broad Range of Cell Types
Multiple, adjustable inspection criteria allow a broad range of cell types and morphologies such as CHO, hybridoma, and cancer cells.

Automated Cell Staining and Mixing
A fully automated, robotic sample and liquid handling system assures precise, accurate sample aspiration, trypan blue mixing and staining, and homogeneity of the cell culture sample.



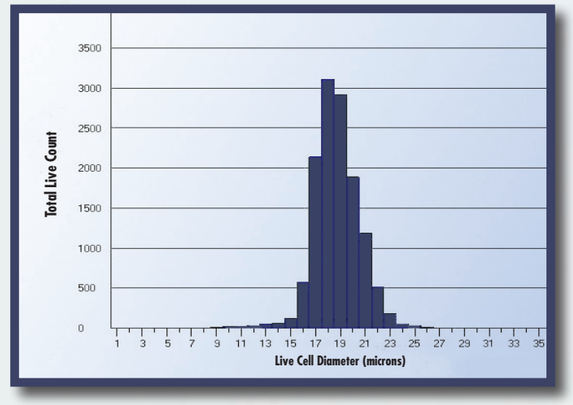
Typical Performance of Total Cell Density Module

Precise Auto Focusing
Cell inspection and counting is initiated after a single, mono-layer of cells settles in the counting chamber. Precise auto-focusing on a mono-layer of cells allows all cells in the image field to be more accurately inspected and classified.

Improved Optical Resolution
Cells remain stationary in the counting chamber as the optics inspect multiple fields. This provides improved resolution compared to inspecting a single field in a flow cell and passing multiple sample aliquots through a flow cell for imaging.

On-Screen Tagging of Viable and Non-Viable Cells
On-screen tagging of viable and non-viable cells allows manual, visual review and confirmation of cell counts.

On-Screen Histograms
On-screen histograms provide a visual display of cell distribution.



Stores Images
Images from the last 30 days can be stored and recalled from memory for re-analysis by new inspection criteria. After 30 days images are stored as jpeg files.

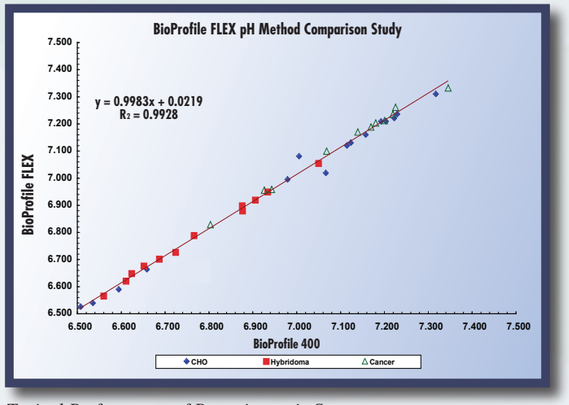
Reduced Blockages and Flow Cell Maintenance
BioProfile FLEX counting chamber geometry is designed to eliminate blockages and flow cell maintenance.

Advanced Analytical Modules Integrated by Robotics

The full 15-test BioProfile FLEX menu is configured in discrete analytical modules that are mechanically and fluidically integrated by robotics. Each BioProfile FLEX module utilizes state-of-the-art technology that is well-proven and characterized in cell culture processes. Building from the Chemistry/Gas Base Module, other modules can be added initially or later in the field.

Chemistry/Gas Base Module
by Electrochemistry

The BioProfile FLEX base module consists of state of the art biosensors for glucose, lactate, glutamine, glutamate, ammonium, pH, PCO_2, PO_2, sodium, potassium, and calcium. Nova biosensor technology has been proven in nearly one thousand BioProfile installations, spanning R & D, process development, pilot, and manufacturing applications worldwide.

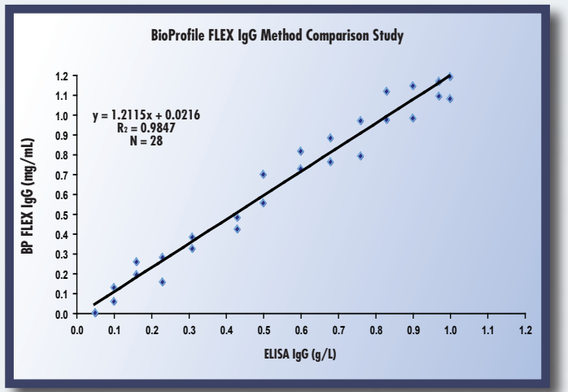


Typical Performance of Potentiometric Sensor

BioProfile FLEX IgG Module
by Photometry

BioProfile FLEX IgG is a rapid, automated method based on the protein affinity of IgG using a colorimetric endpoint detection. This assay is specific to either human or humanized therapeutic IgG of all subclasses. BioProfile FLEX IgG is accurate throughout the range from 0.10 to 5.00 g/L.

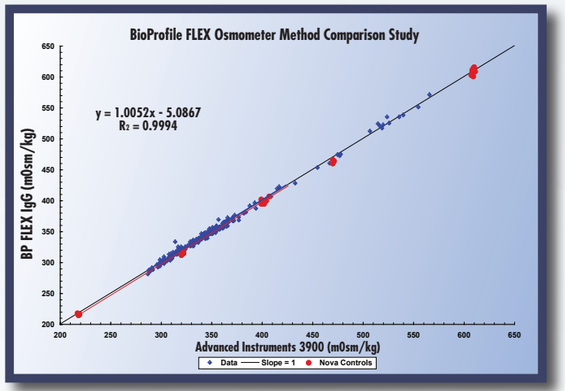
- The analysis time for the IgG module is less than five minutes.
- IgG results can be obtained concurrently with chemistries, cell counts and osmometry on non-centrifuged samples in six minutes.
- BioProfile FLEX reduces the one-day or longer turn around time for a lab analysis of IgG.



Typical Performance of Photometric Module

Osmometer Module
by Freezing Point Depression

BioProfile FLEX uses the freezing point depression method to measure osmolality. A sophisticated robotic sample aspiration and dispensing mechanism improves BioProfile FLEX performance over other osmometers by eliminating technique-prone manual sample pipetting. Sample aspiration is performed automatically from a syringe or sample cup, and a precise sample aliquot is dispensed into the osmometer tray. By automating this manual step, analytical performance is optimized.



Typical Performance of Osmometer Module

Saves Time Labor, and Eliminates Manual Technique Variation

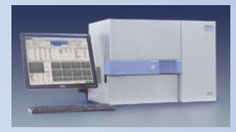
Once the "Analyze" button is pressed, BioProfile FLEX allows complete walkaway automation. A robotic sampling arm and syringe pump aspirate a precise amount of sample, perform any required dilutions, distribute the sample to the modules, and then rinse and prepare for the next sample.

The entire test profile, up to 15 results, is displayed in one report. Data can be automatically stored on BioProfile FLEX or exported to an Excel spreadsheet or data historian.

In addition to eliminating hours of operator time, BioProfile FLEX automation eliminates operator technique errors due to manual calibrating, pipetting, diluting, or data transcribing. Complete automation assures accurate, consistent results from operator to operator, sample to sample, and instrument to instrument.

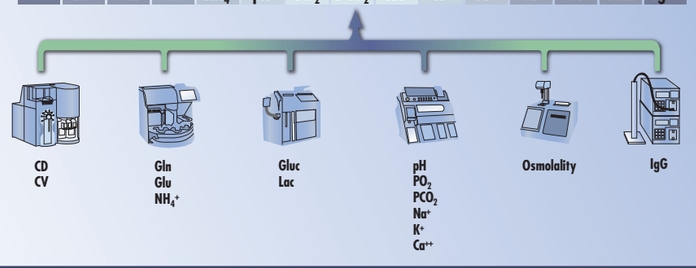
Testing With BioProfile FLEX

- 1-3 operator steps
- 1 minute labor
- 1 mL sample
- 6 minute results for full 15 test panel
- Single data report
- 3 square feet bench space



BioProfile FLEX Test Menu

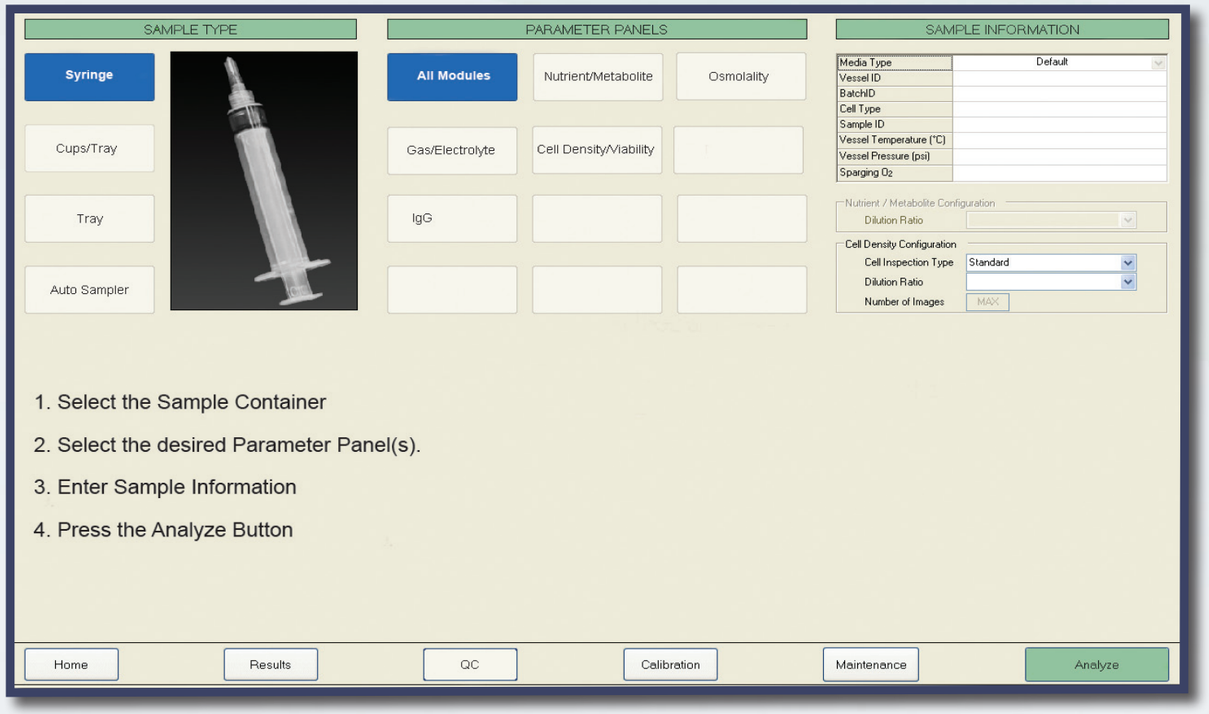
Gluc | Lac | Gln | Glu | NH_4^+ | pH | PO_2 | PCO_2 | Na^+ | K^+ | Ca^{++} | CD | CV | Osm | IgG



Testing Without BioProfile FLEX

- 30 or more operator steps
- 30 minutes labor
- 5 mL of sample
- 24 hours or more for full 15 test panel
- 6 data reports, manual data collating, manual transcribing
- 20 square feet bench space

Intuitive, Easy-to-Use Operator Interface



BioProfile FLEX provides a single, user-friendly touchscreen interface for all modules. Having a common interface for all modules simplifies operation.

- For most users, the home screen will be the only screen needed. Everything needed to log in samples and perform an analysis is on the home screen.
- To further simplify analysis, “one button operation” can be activated using predetermined settings for the sample container, test selection, and sample log-in.

Simple 21 CFR Part 11 Compliance

FDA-regulated Good Laboratory Practice (GLP) and current Good Manufacturing Practice (cGMP) sites that utilize computers for instrument control, data acquisition, data transfer, and archiving must follow 21 CFR Part 11 requirements for electronic records and signatures. BioProfile FLEX provides comprehensive features to assist with meeting these requirements:

Limited Access

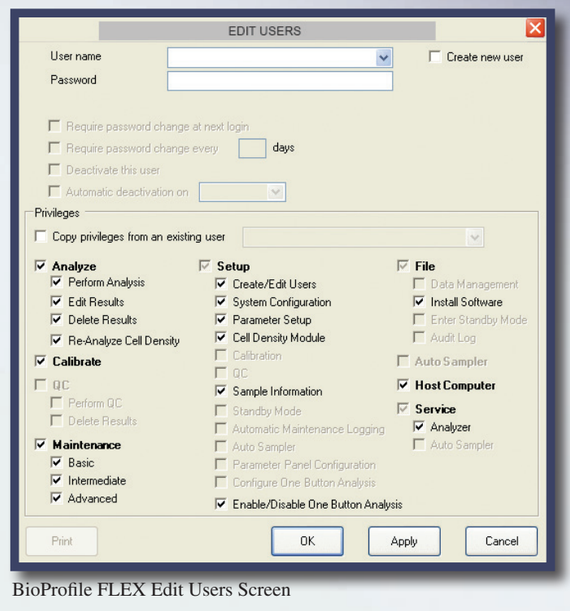
- Administrative password configuration tools limit access to BioProfile FLEX electronic records through password privilege levels.
- User log-on is secured by both user ID and password.
- Automatic log-off features prevent unauthorized access.
- An automatic password de-activation feature is also available.

Electronic Record Retention and Retrieval

- All data are securely and confidentially retained through password access control in both human readable and electronic form.
- Records are readily retrievable throughout their retention period on the BioProfile FLEX analyzer.

Audit Trails

- Time stamped audit trails record the date and time of operator entries and actions that create, modify, or delete electronic records.
- Record changes do not obscure previously recorded information.
- Records are maintained in original and audited form.



BioProfile FLEX Edit Users Screen

Process Analytic Technology (PAT) Compatibility

FDA defines PAT as a system for ensuring final product quality through timely, on-line or at-line measurement and control of critical attributes of manufacturing materials and processes. BioProfile FLEX can be the heart of an automated PAT system to:

Measure

- Provide an understanding of the effects that measurable and controllable attributes such as pH, gases, nutrients, osmolality, IgG, cell density, and cell viability have on final characteristics of the product.

Communicate

- Communicate real time, on-line measurements to other devices such as controllers, plant managers, and data historians.

Capture

- Capture cell culture attributes for review, analysis, and record keeping.

Control

- Provide feedback for control of critical attributes such as pH, nutrients, gases, osmolality, and toxins through bioreactor feedback loops.

R&D, Process Development and Production Applications

Instrumentation for all three environments must be factory rugged, easy to use, and analytically accurate but production use also requires appropriate interface to the factory control system. BioProfile FLEX can deliver consistent accuracy, reliability, and ease of transfer throughout the bio-product life cycle from R&D to full-scale manufacturing.

Easy to Use

- BioProfile FLEX can be operated using a single button. It is easy to use for scientists and production workers alike.
- Operator technique is removed from the testing process.
- Consistent results are obtained from operator to operator, scientist to production worker.

Simplified Validation, Data Analysis, and Archiving

- Consolidating key cell culture parameters in the BioProfile FLEX analyzer simplifies instrument validation, data analysis, archiving, and regulatory compliance.

Compact, Rugged Design

- The BioProfile FLEX footprint saves valuable space compared to the multiple instruments it replaces.
- Its rugged aluminum exterior is capable of withstanding the potentially harsh environment of production facilities.

OPC Interoperability

- The BioProfile FLEX OPC interface communicates with factory control systems, data historians, or laboratory information systems (LIMS).

Minimal Maintenance

- Minimal maintenance requirements make BioProfile FLEX ideal for R&D and production applications alike.
- Snap-in reagents or sensors are easily replaced in minutes.

Customer Support

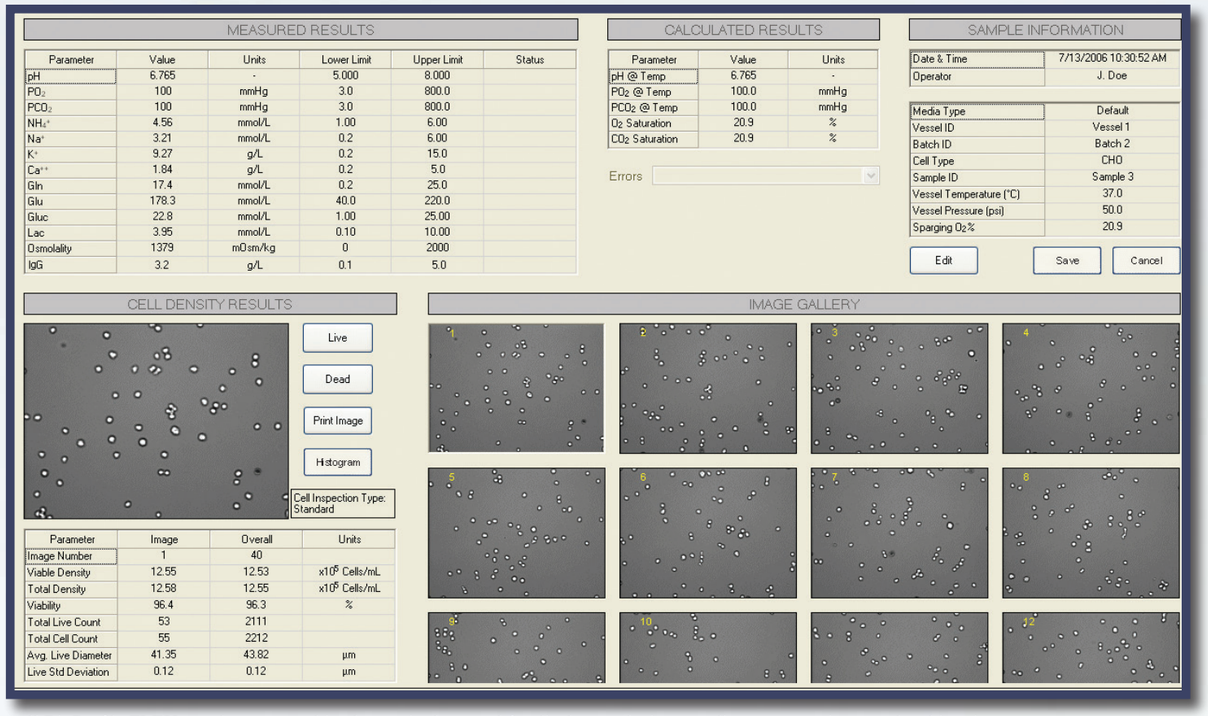
- Nova Biomedical and authorized distributors provide optional comprehensive support for BioProfile analyzers, including:
  - Extensive user training
  - IQ/OQ services
  - Technical assistance
  - Applications assistance

Photo courtesy of Broadley-James Corporation, Irvine, CA and Avid Bioservices. Inc., Tustin, CA

Consolidated Data Report Simplifies Data Analysis and Management

A major difficulty in cell culture monitoring is managing data from a variety of instruments and vendors, and consolidating the data into one repository.

- BioProfile FLEX provides a unified data source for all test parameters. By combining all tests into a single data report, BioProfile FLEX creates an organized data source from scattered data points.
- All test data are available together in one place and at one time, for display, analysis, recording, or exporting to a data historian.
- Scientists are freed from manual methods of data collection and can focus on more important tasks.
- The time and costs of controlling and collating multiple islands of data are reduced.
- A consolidated data source simplifies multivariate data analysis for understanding and identifying process control points.
- Errors due to manual collation of data from multiple instruments are eliminated.
- All BioProfile FLEX data are 21 CFR Part 11 secure. The risk of data loss is reduced. Higher safety and regulatory standards are achieved.



All BioProfile FLEX test data are combined on a single record for display, analysis, recording, or exporting to a data historian.

System Integration Options

BioProfile FLEX with On-Line Autosampler and Sample Retain Collection System

Direct Sampling, Batch Sampling, or On-Line Autosampling

BioProfile FLEX provides multiple options for sampling. These options include individual, off-line or at-line sampling directly from syringes and cups, batch sampling, or fully automated on-line sampling:

Direct Sampling

- Individual samples can be directly sampled from commonly used sample containers including syringes, sample cups, or micro-centrifuge tubes.
- Anaerobic samples can be aspirated from a syringe.

Automated, Batch Sampling

- Fully automated, walkaway batch sampling can be accomplished with the standard BioProfile FLEX 20-position sample tray.
- The tray accommodates both sample cups and centrifuge tubes.

On-Line Autosampling

- An optional On-Line Autosampler connects BioProfile FLEX to as many as ten bioreactors. Scheduling of sampling into the BioProfile FLEX analyzer is user programmable.
- Individual syringe or cup samples can also be analyzed during periods when on-line autosampling is not scheduled.

Advanced OPC Connectivity

The Nova OPC Connectivity Suite integrates BioProfile FLEX with any OPC compliant devices such as bioreactor controllers, data historians, laboratory information management systems (LIMS), and plant management systems. Nova's OPC Connectivity Suite features:

- Automated Bi-directional Flow of Data and Control Commands
- Data Archiving (DA) and Historical Data Archiving (HDA) Capability
- Easy "handshake" connection to any OPC compliant device
- Connectivity verification
- BioReactor Feedback Control
- Remote monitoring of BioProfile FLEX status and data

Sample Retain Collection System

The BioProfile FLEX Sample Retain Collection System is used with the On-Line AutoSampler for automated collection and refrigerated storage of bioreactor samples.

- Retained sample volumes are user selectable from 0.1 to 50 mL
- Removable, insulated sample racks can accomodate thiry-four 15 mL or ten 50 ml conical centrifuge tubes. Two mix or match sample racks can be loaded in the system. The Sample Retain Collector will automatically recognize the type of sample racks loaded in the system.
- Thermo electric temperature storage is user selectable down to a temperature of 3 degrees centigrade.