BIOPROFILE®
FLEX2

Up to 16 cell culture tests in one analyzer: chemistries, gases, cdv, and osmolality

11 chemistry tests with maintenance-free sensor card technology

265 µL combined sample size for full test menu

Measures 16 tests in 4.5 minutes

nova® biomedical

BIOPROFILE® FLEX2

Automated Cell Culture Analyzer with Maint

BioProfile FLEX2 combines Nova's groundbreaking MicroSensor Card™ technology with optical measurement and freezing point osmometry for an automated and comprehensive cell culture analyzer that eliminates chemistry biosensor maintenance, increases analyzer speed, and reduces sample volume. The full, 16-test cell culture menu includes:

Gluc, Lac, Gln, Glu, NH_4^+, Na^+, K^+, Ca^{++}, pH, PCO_2, PO_2, total cell density, viable cell density, viability, cell diameter, osmolality

Compared to the previous generation BioProfile FLEX, there is no maintenance for any of the 11 chemistry and gas sensors (Gluc, Lac, Gln, Glu, NH_4^+, Na^+, K^+, Ca^{++}, pH, PCO_2, PO_2), sample volume is reduced by 75% to 265 µl, and test time is reduced by 50% to 4.5 minutes. Automated sampling from 96-well plates, syringes, or a 24-position external "load-and-go" sample tray as well as a high capacity 48-position osmometer, and direct online autosampling from reactor vessels provides maximum workflow flexibility and efficiency for cell culture monitoring.

Maintenance-free chemistry and gas sensors

Chemistry and gas sensors are combined in the credit-card-sized MicroSensor Card, which uses proven Nova biosensor technology that has been validated in thousands of cell culture processes. Cards are maintenance free, have a minimum use life of 21 days, and are replaceable in seconds.

Cartridge-based reagent management system (RMS)

RMS smart reagent cartridges provide several advantages.

- Cartridge installation date, time, lot number, and expiration data are recorded.
- Reagent usage and status are monitored.
- A self-contained, closed waste receptacle within the cartridge eliminates direct handling of waste and contact with hazardous trypan blue and biological materials. Open systems can pose significant waste handling hazards to operators.

enance-Free Chemistry and Gas Sensors

Fast analysis time

Test results for the complete menu including cell density/viability, pH/gases, and key chemistries are available in 4.5 minutes. Throughput for individual modules is as fast as 120 seconds.

Small sample volume

Sample volume is 265 µL for a full, 16-test profile, enabling comprehensive testing even from low volume culture systems. Individual modules require as little as 135 µL.

Analysis time and sample size when modules are run individually

Module	Analysis Time	Sample Size
Chemistry Module: Gluc, Lac, Gln, Glu, NH_4^+, Na^+, K^+, Ca^{++}	120 sec	135 µL
Osmometer Module: Osmolality	240 sec	135 µL*
Cell Density/Viability Module: Total cell density, viable cell density, viability, cell diameter	220 sec	135 µL
Gas Module: pH, PCO_2, PO_2	120 sec	265 µL

Analysis time and sample size when modules are run collectively

All Modules-All Tests	270 sec	265 µL*

* Additional 10µL required with OSM48 module

BIOPROFILE® FLEX2

Maximum Workflow Efficiency

Intuitive user interface

Simple touchscreen operation, a choice of three sampling modes, fast analysis time, and automated quality control (QC) provide simplicity, labor savings, and workflow efficiency for cell culture monitoring.

The color touchscreen is easily operated with intuitive prompts and requires minimal training.

- Navigate the most commonly used function screens with a single click.
- Batch assignment of sample information and test panels makes programming 96-well plates and sample trays fast and eliminates errors in setup.

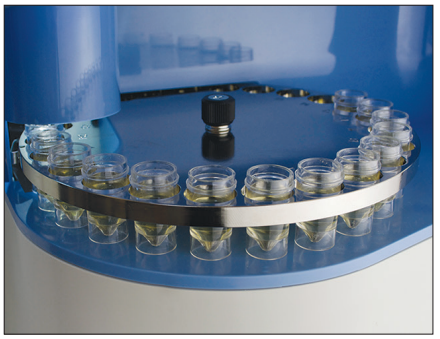
Onboard automated quality control

Onboard liquid QC provides true verification of FLEX2 performance and saves hours of labor each week compared to manual QC testing. QC cartridges contain up to a 30-day supply of QC material. Controls are run automatically at user-selected intervals.

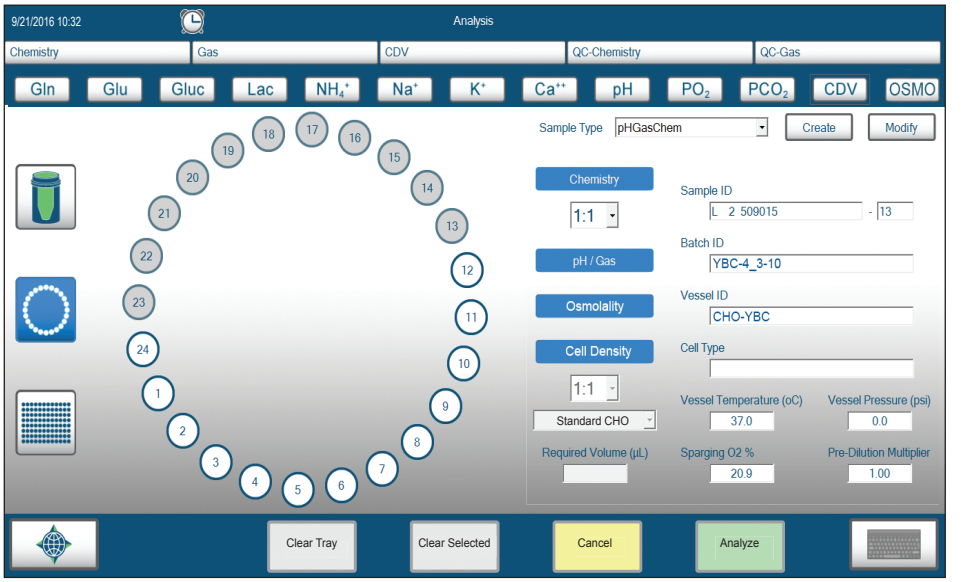
Supplemental quality monitoring (SQM)

As a supplement to liquid QC, SQM electronically monitors the status and performance of all analytical components (including sensors, reagents, calibrators, sample conditions, software, and electronics) providing real-time, sample-to-sample assurance of analyzer performance.

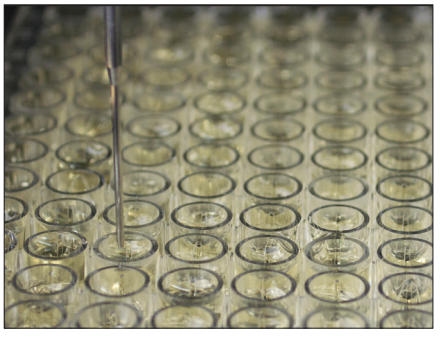
24-position external load-and-go tray



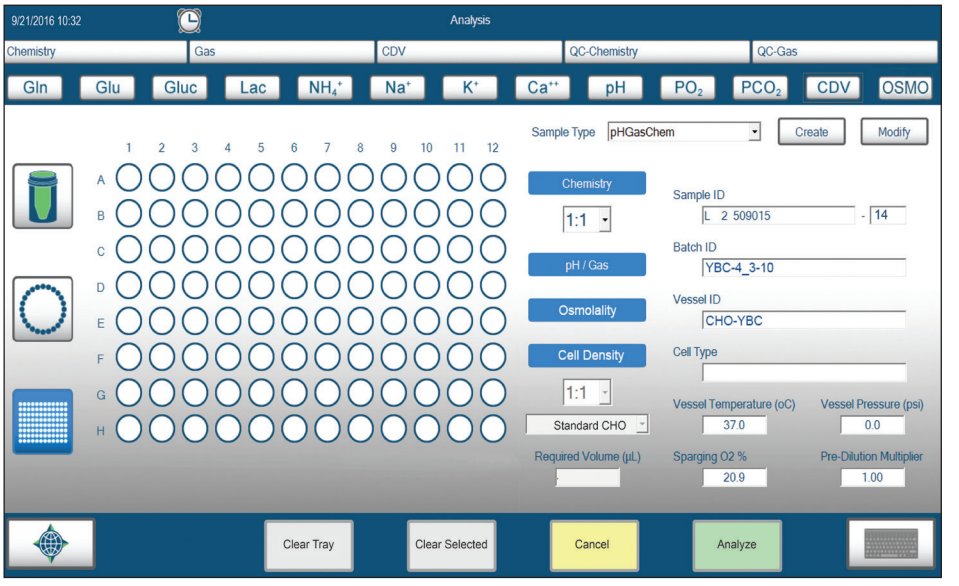
An external load-and-go sample tray allows for continuous loading of cell culture samples for flexible and efficient sample throughput.



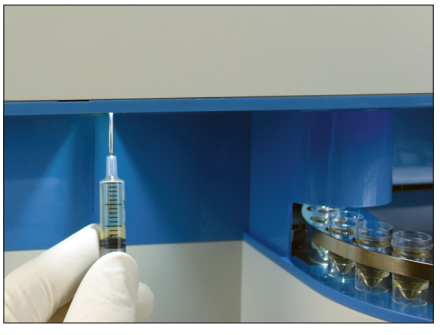
Automated 96-well plate analysis



FLEX2 is the only cell culture chemistry analyzer to offer automated sampling from 96-well plates.



Syringe or cup sampling for critical analysis



Individual samples also can be analyzed directly from syringes or cups. Batch sampling via the 96-well plate and/or the external load-and-go sample tray can be interrupted at any time to run critical samples.

BIOPROFILE® FLEX2

Advanced Analytical Modules

FLEX2's test menu is configured in advanced modules that are integrated with robotics. Each module utilizes state-of-the-art technology that has been proven and characterized in cell culture processes.

Chemistry module

by electrochemistry

The chemistry module consists of electrochemical biosensors for glucose, lactate, glutamine, glutamate, ammonium, sodium, potassium, and calcium, integrated into one credit-card-sized component.

Broad analytical range with improved low end accuracy

The lower analytical range has been extended to provide accurate results down to 0.10 g/L for glucose/lactate and 0.10 mmol/L for glutamine/glutamate.

Onboard auto-dilutions

Robotic automation and a precise, metering syringe pump perform all dilutions on board, eliminating time-intensive manual dilutions and error associated with manual techniques. The use of onboard auto-dilutions provides the broadest analytical range of any cell culture analyzer.

Chemistries are unaffected by cell concentration

Photometric detection methods used by other analyzers often require time-consuming, manual pre-dilution of the sample to avoid poor measurement accuracy due to high cell concentrations. FLEX2 provides accurate results regardless of cell concentration.

Analyte specificity

Nova's biosensors are developed specifically for cell culture applications, where processes typically utilize extremely complex media formulations. These electrochemistry detection methods provide excellent specificity for the analyte of interest.

High throughput chemistry analysis

The chemistry module is capable of analyzing a full chemistry panel using 135 µL of sample in 120 seconds, or a throughput of 30 samples per hour. Full 96-well plates can be analyzed in about three hours.

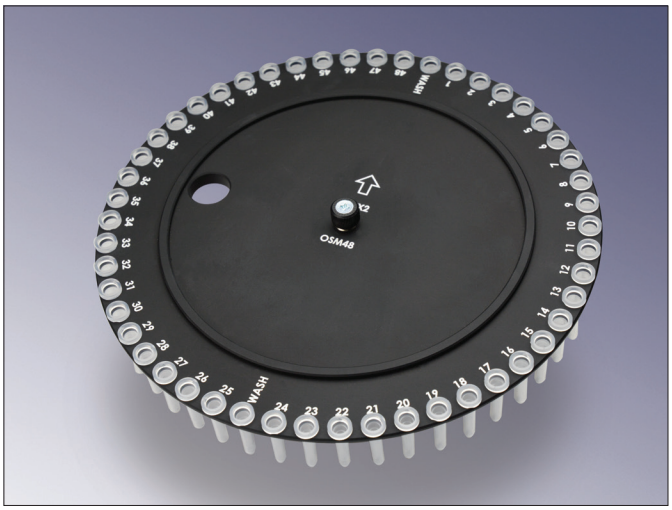
High capacity, 48-position Osmometer module

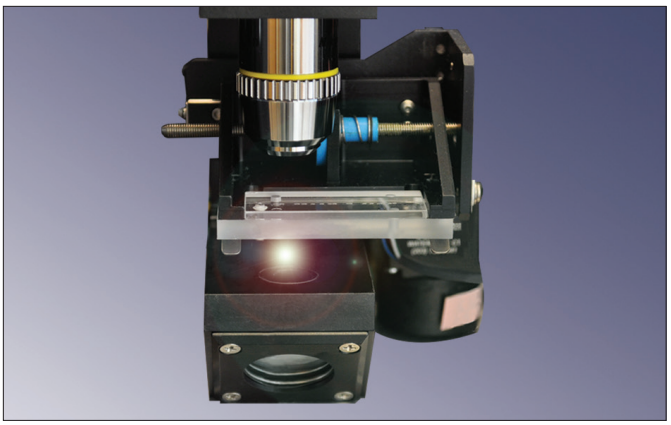
by freezing point depression

Freezing point depression osmometry is considered the gold standard for measuring osmolality in cell culture processes. FLEX2's sophisticated robotic sample aspiration and dispensing mechanism improves performance over other osmometers by eliminating error associated with manual sample pipetting.

Walkaway automation

FLEX2's high capacity, 48-position osmometer enables walkaway, automated sampling of up to 48 samples without any user intervention, significantly prolonging maintenance intervals. The high capacity tray also enables completely automated sampling for all tests, including osmometry, for automated culture systems such as the Sartorius ambr®15. This eliminates the need to replace osmometer tubes in the middle of a sampling set and allows for sample scheduling in the middle of the night, on weekends, and holidays, without the need to perform any maintenance during the full batch of automated samples. This capability frees the instrument to perform regular sampling of non-automated cultures during normal business hours.





FLEX2's high resolution optics count cells as small as 4 microns

Cell density, cell viability module

by high resolution digital optics

Cell density and cell viability are measured by an automated trypan blue exclusion method combined with high resolution digital optics and advanced software algorithms. Cell counting accuracy and precision are optimized in several ways:

Automated dilutions

FLEX2 requires no manual dilutions for cell density analysis up to 160,000,000 cells/mL. The optics maximize precision and accuracy by eliminating manual dilution steps, which can add variability to cell counting results.

Wide range

A wide range of cell densities from 100,000 to 160,000,000 cells/mL can be counted, even with cells as small as 4 microns.

Counts up to 45 optical fields

FLEX2 counts up to 30 times more cells than other commonly used counting methods. Accuracy and validity of the cell count is improved by the larger number of cells counted.

Automated cell staining and mixing

A fully automated, robotic sample and liquid handling system ensures precise and accurate sample aspiration, trypan blue staining, and homogeneity of the cell culture sample.

Broad range of cell types

Multiple, adjustable inspection criteria allow for the counting of a broad range of cell types and morphologies, including CHO, hybridoma, and insect cell lines.

Image of histogram

On-screen histograms provide a visual display of live cell diameter distribution.

Stores images

Images from the last 60 days can be stored and recalled for review or re-analysis. After 60 days, images are stored as jpeg files but remain available indefinitely for viewing. Data is never destroyed or automatically removed from the system's database.

Gas module

by electrochemistry

The gas module consists of biosensors for pH, PCO_2, PO_2. They are located in the MicroSensor Card.

Improved accuracy

Unlike hospital blood gas analyzers, which are often used for cell culture analysis, Nova's algorithms for measuring pH, PCO_2, and PO_2 were specifically developed for cell culture applications. These algorithms are optimized for mammalian cultures that typically exhibit much higher oxygen consumption and carbon dioxide production rates compared to human blood cells. FLEX2 ensures accurate pH and gas values even in cultures with high cell densities.

Gas and pH values available in manual and load-and-go tray analysis modes

FLEX2 allows the user to configure the gas module to provide gas and pH results from both manual samples and the external carousel tray.

BIOPROFILE® FLEX2

Fully Automated Sampling Options

FLEX2 Automated Cell Culture Analyzer

Sample Transfer Module (STM)

Automated Sample Retain Collector

Reactor Sampling Module (RSM)

On-Line Autosampler System

The FLEX2 On-Line Autosampler (OLS) is a modular system for automated sampling and analysis of key cell culture analytes. The OLS small sample volume and fast analysis time provide automated sampling and analysis from 10 bioreactors in less than 1.5 hours and setup can be completed in less than 20 minutes. An OLS typically has from 1-10 remote sampling modules (one for each bioreactor), one Sample Transfer Module for up to 10 bioreactors and a Sample Retain Collector. See the BioProfile FLEX2 On Line Autosampler brochure for details.

Nova's OLS provides fully automated sampling from virtually all culture systems from single-use bench scale bioreactors to large production bioreactors. When connected to an OPC-compatible control system, FLEX2 OLS provides real-time data transmission for automated sampling, analysis, and feedback control of all measured parameters.

FLEX2 can also automatically deliver cell culture samples from ambr® 15 and ambr® 250 microbioreactor systems for analysis using the optional External Sampling Module (ESM).

Rapid analysis, real-time data collection, accelerated timelines

FLEX2 OLS provides real-time data collection and the ability to automate up to 24 sample measurements per culture each day, enabling rapid process characterization and accelerated timelines.

Feedback control

FLEX2's automation enables full feedback control of all measured parameters, including pH. FLEX2 data can be used to deliver precise glucose feeding strategies, ramp perfusion rates based on cell density, and generate one-point pH probe calibrations, to name just a few of the many automation functions enabled with a FLEX2 automated cell culture system.

Labor and cost savings per day

BioProfile FLEX2's automation saves up to eight hours per day of manual sampling, sample analysis, data collection, and data management. Errors are virtually eliminated by automating all sample handling, analysis steps, and data management.

On-Line sampling for ambr® 15 and ambr® 250 cell culture systems

FLEX2 Automated Cell Culture Analyzer and External Sampling Module (ESM)

ambr® 15 cell culture Microbioreactor System

FLEX2 with a single ESM fully automates sampling of a complete ambr® 15 or ambr® 250 cell culture system. While configured with an ESM, FLEX2 can still be used for manual and tray sampling.

BIOPROFILE® FLEX2

Connectivity, Compliance and Support

Open Platform Communications (OPC) connectivity

Nova's OPC connectivity integrates FLEX2 with any OPC-compliant device, such as bioreactor controllers, data historians, laboratory information management systems (LIMS), and plant management systems. Nova's OPC connectivity features:

- Automated bidirectional data and control commands
- Data archiving
- Connection to any OPC-compliant device
- Connectivity verification
- Bioreactor feedback control
- Remote monitoring of status and data

GMP compliance

FLEX2 meets GMP manufacturing requirements through installation qualification (IQ), operational qualification (OQ) and validation support from Nova specialists.

Compliance with 21 CFR Part 11

Limited access

User log-on is secured by both user ID and password. Automatic log-off features prevent unauthorized access.

Electronic record retention and retrieval

- All data are securely retained through password access control in both human-readable and electronic forms.
- Records are readily retrievable throughout their retention period.

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.

Support Services

The purchase of a FLEX2 analyzer is just the beginning of a long commitment from Nova to you. There is an extensive array of support services to help maintain peak analyzer performance.

Installation

Performed by a Nova field specialist, installation consists of analyzer setup and performance verification.

Validation assistance

Nova installation staff can perform extended precision and reference analyzer correlation studies. Nova performs all tests and provides complete documentation to verify compliance to regulatory standards. In addition to IQ/OQ support, we can assist with performance qualification (PQ) protocol development and implementation.

Field service

On those occasions when service is needed, a team of field service representatives, located throughout the country, is available to provide on-site support, resolving issues with minimal downtime.

Comprehensive applications services

A knowledgeable applications staff with significant industry experience is available to help with custom optimizations, IQ/OQ, process automation support, and other site-specific needs.

Telephone assistance hotline

We maintain a highly skilled and experienced technical support staff available by phone or email. From basic questions to advanced troubleshooting, they are able to resolve most problems over the phone without requiring on-site support.

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Specifications

Sample Analysis Time:
2.0 minutes (Chemistry only)
2.0 minutes (Gases only)
3.8 minutes (Osmolality only)
4.0 minutes (Cell Density/Viability only)
6 minutes (On-Line Autosampler, Chemistry only)
8.5 minutes (On-Line Autosampler, All modules)
Operating Temperature Range..... 15°C to 30°C (59°F - 86°F)
Operating Relative Humidity Range..... 20–85%
Sample Size ..... 135 to 275 µL

Sample Options:
Individual via syringe/cup
Automated batch using 24-position tray or 96-well plates
Automated online using FLEX2 On-Line Autosampler
Operating System ..... Windows 10
Electrical Requirements..... 90-264 VAC, 50 to 60 Hz
(Universal Power Supply)

System Size and Weight:
Height: 24 in (61 cm), Width: 17 in (43 cm), Depth: 25 in (64 cm)
With optional osmometer module:
H: 24 in (61 cm), W: 25 in (64 cm), D: 25 in (64 cm)
94 lb (42.6 kg) without reagent packs

Certifications:
IEC 61010-1:2010, OPC Compliant, PAT Compatible, 21 CFR Part 11 Compliant

FLEX2 with Osmometer Module

Chemistry/Gas Module

Assay	Measurement Range	Resolution	Method
Glucose	0.10–60.00 g/L*	0.05 g/L	Biosensor
Lactate	0.10–24.00 g/L*	0.05 g/L	Biosensor
Glutamine	0.10–24.00 mmol/L*	0.05 mmol/L	Biosensor
Glutamate	0.10–24.00 mmol/L*	0.05 mmol/L	Biosensor
Ammonium	0.20–100.00 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	3.0–500.0 mmHg	0.1 mmHg	Clarke Electrode
Sodium*	40.0–1200.0 mmol/L*	0.1 mmol/L	Direct ISE
Potassium*	1.00–400.00 mmol/L*	0.01 mmol/L	Direct ISE
Calcium*	0.10–40.00 mmol/L*	0.01 mmol/L	Direct ISE

*Ranges reflect user-selectable onboard 1:4 dilution

Calculated Tests:
O_2 Saturation; CO_2 Saturation; HCO_3 -(bicarbonate), Temp. Corrected pH, PCO_2, PO_2

OSM48 Osmometer Module

Assay	Measurement Range	Resolution	Method
Osmolality	0–2000 mOsm/kg	1 mOsm/kg	Freezing Point Depression

OSM20 Osmometer Module

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

Cell Density/Viability Module

Assay	Measurement Range	Resolution	Method
Cell Diameter	4.00–70.00 µm	0.01	Digital Imaging
Density	$1.00e^{+05}$–$1.60e^{+08}$ cells/mL**	1	Digital Imaging
%Viability	0.0–100%	0.1	Digital Imaging

**Density range reflects user-selectable onboard 1:6 dilution

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Specifications current as of revision date.

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