Ambr® Analysis Module

pH Calibration and Raman Spectroscopy Integration
Ambr® Analysis Module

Automates pH Calibration and Raman Spectroscopy for Ambr® Bioreactors

The Ambr® Analysis Module provides add-on capability for automated measurement of pH and Raman spectroscopy for Ambr® 15 and Ambr® 250 High Throughput bioreactors. The pH measurement automates initial bioreactor vessel pH sensor calibration and subsequent in-process recalibration, and eliminates the operator time needed for manual offline pH measurement, data transfer and bioreactor pH sensor recalibration.

**Ambr® Analysis Module Benefits**
- Full automation of pH measurement sampling and assay
- Reduced CO₂ outgassing effects and errors compared to manual off-line pH sampling
- Automated accurate pH sensor recalibration
- Optimised pH measurement modes for normal and high cell density cultures
- Allows integration of 3rd party Raman spectroscopy probes and data flows
- User replaceable pH sensors, Raman flow cells, and reagent kits

The Ambr® Analysis Module is suitable for use with both cell culture and microbial media and supports two user-selectable measurement modes for cell cultures up to at least 100 million cells/mL. It is not suitable for cultures containing particulates (beads or microcarriers, for example) or highly viscous samples.

BioPAT® Spectro in Ambr® has been tested with CHO cell cultures but not microbial cultures. BioPAT® Spectro in Ambr® is suitable for use with mammalian fed-batch cell cultures but has not been evaluated with high cell density perfusion cultures.

**pH Calibration Performance**
- Accurate, precise, linear response when reading a range of pH buffers
  \[ y = 0.9998x \quad R^2 = 0.9999 \]

**Ambr® Analysis Module Benefits**
- Accurate, precise measurement of CHO culture pH
- Ambr® 15 CHO culture
- \( N = 24 \) bioreactors, \( \sim 10^6 \) cell/mL at day 6
- Reference measurement: Calibrated electrode inserted into Ambr® 15 vessel

Find out more
## Specifications

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ambr® 15</th>
<th>Ambr® 250 High Throughput</th>
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</thead>
<tbody>
<tr>
<td>Sample volume, pH</td>
<td>60 µL</td>
<td>200 µl</td>
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<tr>
<td>Sample volume, BioPAT® Spectro</td>
<td>110 – 200 µl</td>
<td>110 – 200 µl</td>
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<tr>
<td>Cycle time per reading, pH</td>
<td>160 s</td>
<td>160 s</td>
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<tr>
<td>Cycle time per reading, BioPAT® Spectro</td>
<td>5 – 15 min</td>
<td>5 – 15 min</td>
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<tr>
<td>pH Resolution</td>
<td>0.01</td>
<td>0.01</td>
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<tr>
<td>BioPAT® Spectro in Ambr® requirements</td>
<td>Compatible Kaiser/Tornado Raman spectrometer and BioPAT® Spectro probe. Appropriate SIMCA® license (not included). Win10 Ambr® control PC.</td>
<td></td>
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</table>
BioPAT® Spectro in Ambr® enables the automated integration of Raman spectrometers from Kaiser Optical Systems and Tornado Spectral systems, via a Sartorius-specific fiber optical probe.

### BioPAT® Spectro in Ambr® Benefits
- Automated consolidation and contextualization of all spectral and process data into a SIMCA®-ready file for model building
- Ambr® derived Raman models are more robust due to the use of all process data, a large DoE design space, and automated spiking of Ambr® samples with analyte stock solutions
- Ambr® can use SIMCA® models to predict analyte concentrations and execute process control in real time

### BioPAT® Spectro in Ambr® Performance
- A model building Ambr® 250 High Throughput run (N=8) was carried out using a Cellca2 CHO mAb process
- >200 data points were automatically assayed by integrated BioProfile FLEX2 and an integrated Raman analyzer
- Raman, FLEX2 and Ambr® process data were automatically collated in the Ambr® software
- A separate copy of SIMCA® software was used to build a Raman glucose model

- A second Ambr® 250 High Throughput Cellca2 run (N=12) was carried out to assess process performance based on real-time Raman predictions (N=6) in comparison to integrated FLEX2 (N=6)
  - (A) Raman glucose predictions matched very closely to FLEX2 measurements (N=1 shown for clarity)
  - (B) Cell culture profiles were very consistent and equivalent for glucose control based on either integrated Raman (N=6) or FLEX2 (N=6) analyzers

Find out more
A. Glucose measurement using Raman Prediction vs integrated FLEX2

B. Glucose control using Raman Prediction vs integrated FLEX2
BioPAT® Spectro Platform
Meeting the Needs of Process Development and Commercial Manufacturing

Find out more
Ambr® 15 Cell Culture

Ambr® Analysis Module

Computer

Raman spectrometer

and controller

BioPAT® Spectro in Biostat STR®

Optical probe

Liquid circulates through BioPAT® Spectro single-use port

Ambr® computer

Raman spectrometer and controller

Biostat STR®

SCADA / DCS

Spectrometer control software

Ambr® 250 High Throughput
Operation of the Ambr® Analysis Module is supported by replaceable sensors, a replaceable BioPAT® Spectro flow cell, and reagent kits including calibration solutions, cleaning solutions and a waste container. The ability to reliably measure pH is process, cell line, and cell density dependent. It is recommended pH and Reference sensors be replaced at least every 3 months. Actual lifetime will be dependent on process application and may necessitate more frequent replacement.

BioPAT® Spectro flow cell for Ambr® Analysis Module

pH and reference electrodes

Reagent kit, pH

Consumables