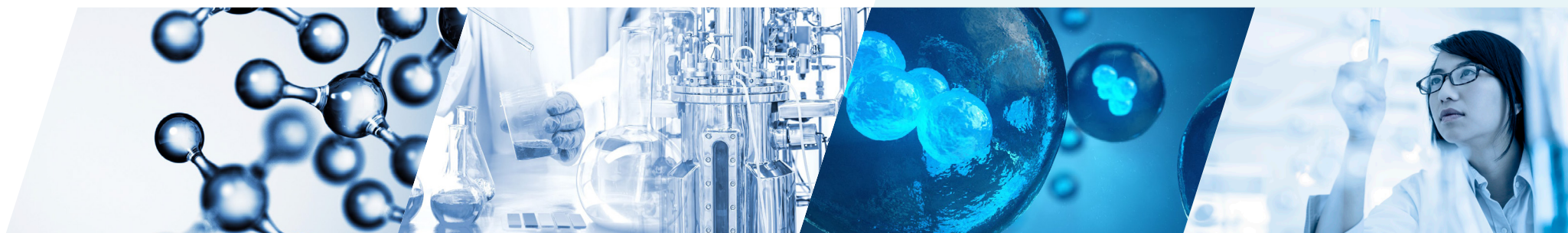




A guide to improving biotech processes with gas analysis mass spectrometry



Table of contents



Overview

- What is a PAT program?
- Why gas analysis?
- Process mass spectrometer gas analysis applications
- Real-time monitoring of fermentation and cell cultures
- Gas analysis in mammalian cell culture processes
- At-line and in-process monitoring in pharmaceutical manufacturing

Technology

- Overview of how process mass spectrometers work
- Scanning magnetic sector technology Analog scans
- Rapid Mult-Stream (RMS) sampling Stream status
- Prima BT and Prima PRO Process Mass Spectrometers with GasWorks® interface
- EffecTech validation
- Service for Prima Process Mass Spectrometers

Resources

- Peer-reviewed research paper
- On-demand webinar
- Integrated software

Learn more

- Generating reliable quantitative solvent drying process data in the pharmaceutical industry
- About Thermo Fisher Scientific
- Speak with a representative

What is a PAT program?

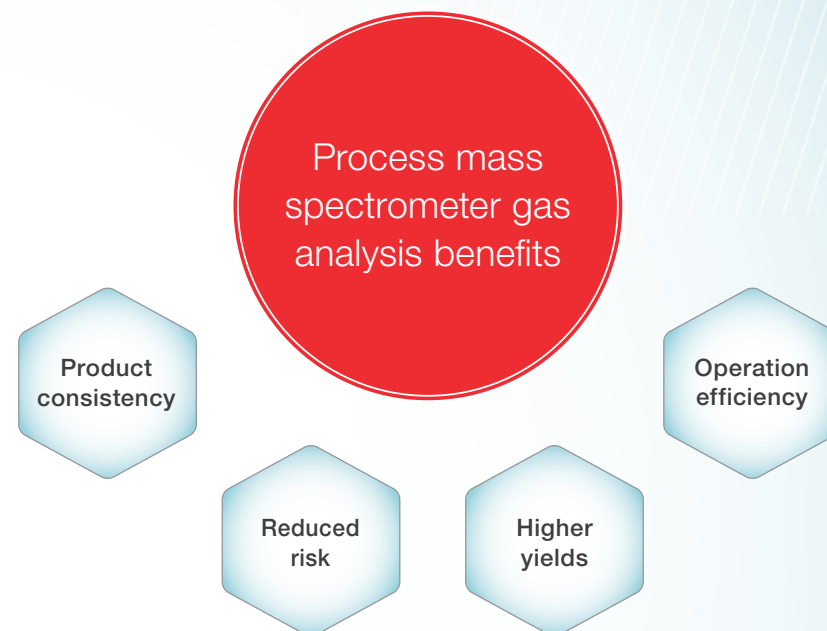
The FDA's Process Analytical Technology (PAT) initiative promotes improved process understanding by defining Critical Process Parameters (CPP) and monitoring these CPPs, either in-line or on-line. Processes can become more efficient, with reduced over-processing and greater product consistency. Gain productivity by instituting a PAT program that is simple, data-rich, and low-risk.



Why gas analysis?

Monitoring critical process parameters (CPP) with process mass spectrometry gas analysis provides many benefits.

- Track batch progress in real-time
- Pinpoint contamination and maximize viable cell mass to increase profits
- Reduce over-processing/waste
- Increase product consistency with fault-tolerant operation
- Reliably monitor the composition of gas streams into and out of fermenters and bioreactors



Click [here](#) to watch the video, *Off-gas monitoring in fermentations with Prima Mass Spectrometers*



Process mass spectrometer gas analysis applications



[Click here](#) to view infographic,
*Five reasons to use process mass
spectrometry in biotechnology*



Real-time monitoring of fermentation and cell cultures

Process mass spectrometers for continuous analysis of respiratory gases

- Characterize fermentation and cell culture processes
- Non-invasive technique available for multiple sample points (up to 60)
- Track growth kinetics and substrate consumption
- Determine the endpoint for maximum product yield
- Precise measurement of Oxygen Uptake Rate (OUR), CO₂ Evolution Rate (CER) and Respiratory Quotient (RQ)

The speed of MS makes it ideal for fermentation and cell culture applications, but speed must not be at the expense of precision. It is equally important that precise data is acquired; otherwise, small changes in concentration will be lost. Over 30 years of industrial experience have shown that magnetic sector analyzers offer the best performance for fermentation off-gas analysis. Key advantages include improved precision, accuracy, long intervals between calibration, and resistance to contamination.

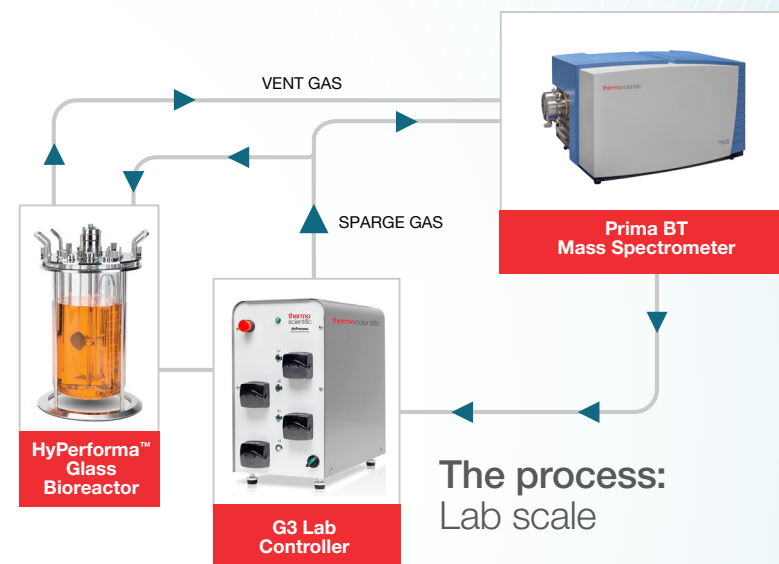


[Click here](#) to download the application note,
*Gas analysis mass spectrometer applications in
fermentation and cell culture process*



Gas analysis in mammalian cell culture processes

In cell cultures, it is essential to monitor the state of the cultures since its health determines the conversion rate of nutrients, the formation of unwanted by-products, and, in the worst case, the onset of poisoning. Analysis of the respiratory gases being fed into and produced from the cell culture is an ideal way of characterizing the behavior and productivity of the cells during the process. It is non-invasive and enables monitoring of the physiological state of the culture, including growth kinetics and substrate consumption. It also helps determine the optimum point to halt the process for maximum yield.



[Click here](#) to download the gas analysis in mammalian cell culture processes solutions brochure



Generating reliable quantitative solvent drying process data in the pharmaceutical industry

Industrial process mass spectrometer for monitoring of multiple solvents from up to 10 dryers

- Monitor and characterise drying stages
- Improve consistency and quality of the final product
- Reduce drying times, increase throughput and maximize profitability
- Avoid over-drying

A key production stage that has received a great deal of attention is the drying process, the complete or partial removal of a solvent or solvents from an Active Pharmaceutical Ingredient (API) or intermediate. Gas analysis mass spectrometry has been used extensively on a wide range of dryers, including filter dryers, vacuum dryers, tray dryers, rotary dryers, and spray dryers.



[Click here](#) to download the application note, **Generating reliable quantitative solvent drying process data in the pharmaceutical industry**

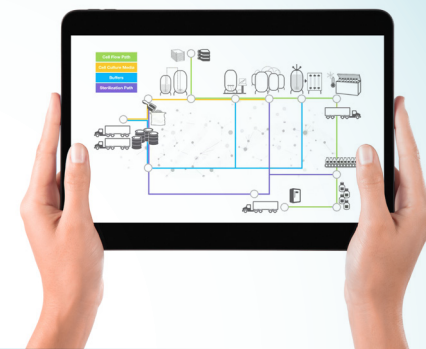


At-line and in-process monitoring in pharmaceutical manufacturing

Controlling manufacturing by testing and measuring during the processing of critical quality and performance attributes of raw and in-process materials helps ensure final product quality. Real-time off-gas monitoring provides metabolism data while reducing the need for offline testing and without compromising the sterile environment. With advanced process mass spectrometers, biotechnology companies can monitor and control multiple fermenters in real-time to ensure that each progresses according to the design of the experiment and produces optimum outcomes.

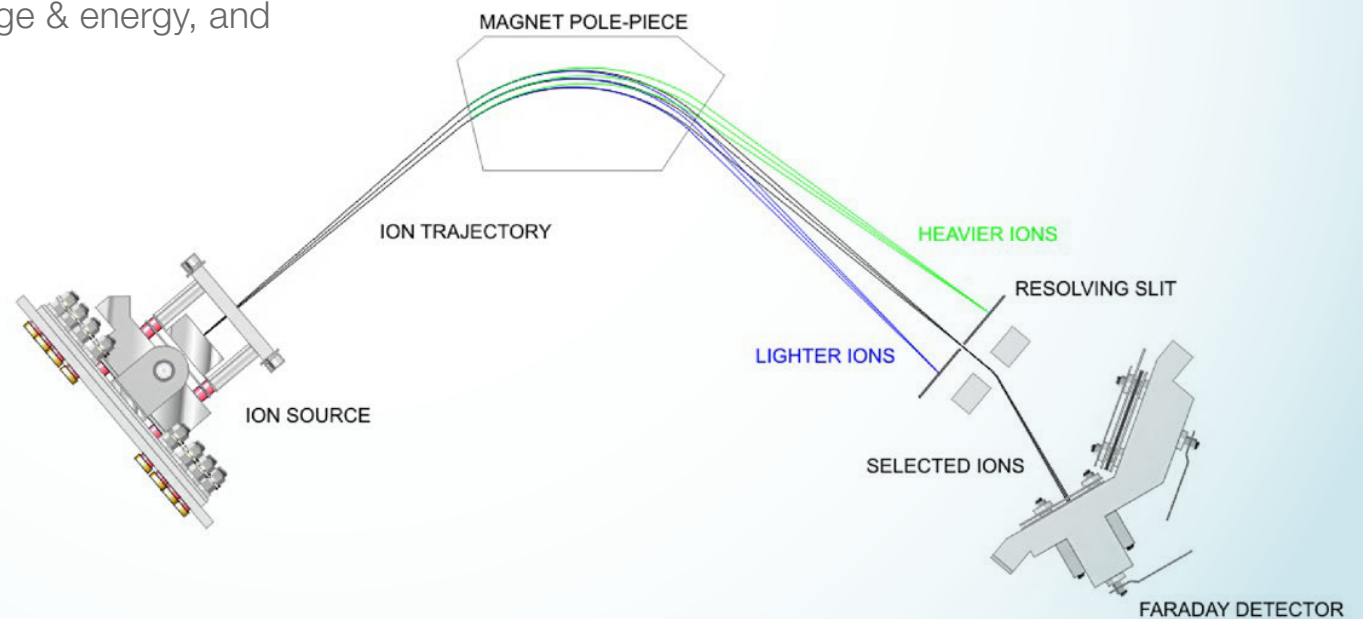


[Click here](#) to see process map for pharmaceutical and biotech manufacturing



Overview of how process mass spectrometers work

- Sample gas (here, N_2 and O_2) enters the ion source and is converted to positive ions by collision with high-energy electrons from the filament
- N_2 is ionized to N_2^+ at 28 AMU, O_2 is ionized to O_2^+ at 32 AMU
- Ions are accelerated into the variable magnetic field and move in a circular path
- Radius depends on the ion's mass, charge & energy, and magnet field strength
- Vary magnet field strength—bring ions sequentially onto a single detector
- Detector output is directly proportional to the concentration
- Magnetic sector analyzer produces characteristic flat top peak—consistent intensity across the whole peak

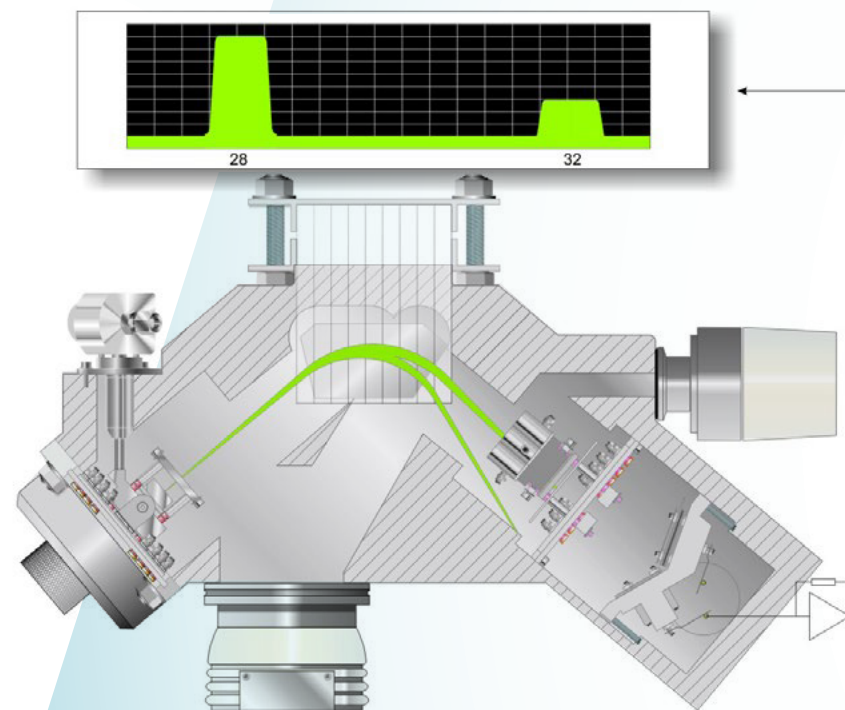


Scanning magnetic sector technology

The primary feature of this process analyzer is the scanning magnetic sector technology. This field proven technology has demonstrated the highest performance for online gas analysis.

Scanning magnetic sector analysers offer high precision, accuracy, long intervals between calibrations, and resistance to contamination. Typically, analytical precision is between 2 and 10 times better than a quadrupole MS, depending on the gases analyzed and the sample composition, long term resistance to contamination ensures continued operation without any requirement to interrupt the analyzer for mass filter cleaning.

The signal intensity at any specific mass position appears as a symmetrical flat topped peak, negating the need to measure at the exact middle of the peak. Any small drift in mass position will not result in a change in signal intensity.



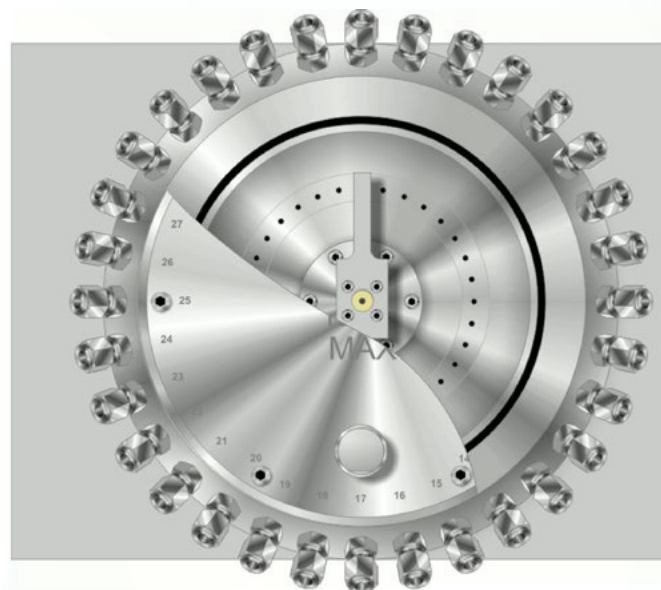
Fault tolerant design to increase uptime

Rapid Multi-Stream (RMS) sampling

The unique Rapid Multi-Stream (RMS) inlet system allows for the selection of 16 to 64 streams and sets new standards for speed and reliability of multi-stream sampling and maintenance intervals. Avoid extra maintenance of multiple instruments and rely on one process mass spectrometer to analyze up to 64 sample gas points. Combining two RMS enables sampling from more than 100 points.

The RMS is not a rotary valve allowing all gas streams to flow continuously. The position of the rotating arm is optically encoded for reliable computer-controlled stream selection. Downstream of the RMS is a digital flow sensor to report sample flow for each selected sample point.

A simple analysis of six gases has a 10-second completion time. A more advanced analysis of 40 gases has a 30-second completion time. The user has the ability to select the most efficient peak measurements for each analysis as well as the appropriate speed, depending on the process control requirements. The software's stream status keeps the user informed of the analysis.



Prima BT and Prima PRO Process Mass Spectrometers with GasWorks interface

Highly reliable and easy-to-own, Thermo Scientific™ Process Mass Spectrometers deliver faster, more complete, lab-quality online gas composition analysis.

- Highly reliable
- Precise multi-component analysis
- Concentrations of respiratory gases, inerts, and volatiles can be measured in seconds
- 16, 32, or 64-port Rapid Multistream Sampler (RMS) for fast, reliable monitoring of multiple fermenters and bioreactors
- 21 CFR Part 11 compliant Thermo Scientific™ GasWorks® Software. Rapid installation to facilitate ongoing operation while providing a secure, stable platform for process analytics



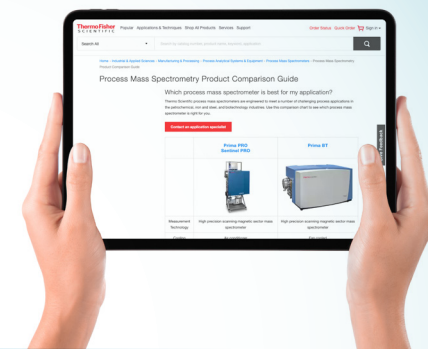
Lab scale:
Thermo Scientific Prima BT



Production scale:
Thermo Scientific Prima PRO 710



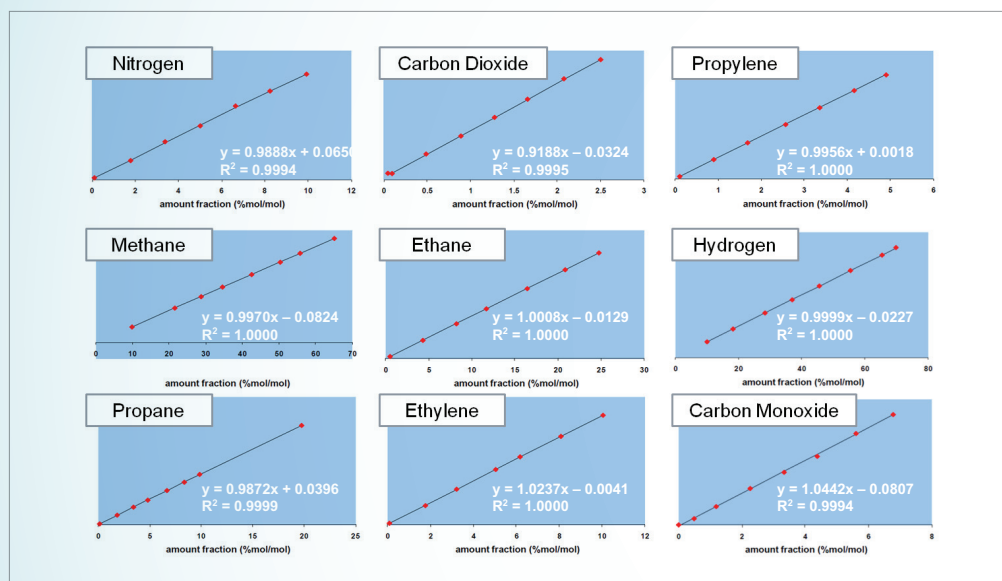
[Click here](#) to view the process mass spectroscopy product comparison guide



EffecTech validation

The scanning magnetic sector in the Prima PRO is laminated to scan at speeds equivalent to that of quadrupole analyzers, offering the unique combination of rapid analysis and high stability of an unlimited number of user-defined gases.

Independent testing at the world-renowned and accredited test authority EffecTech validated the unrivaled accuracy of the Prima PRO for a range of common gas species over wide dynamic ranges.



The performance benchmarks of this instrument were calculated over the following maximum expected composition range when used in combination with an ISO 17025 accredited calibration gas.

Component	Calibration gas ¹ (% mol/mol)	Sample composition range ² (% mol/mol)	
		Minimum	Maximum
Nitrogen	9.000 ± 0.015	0.10	9.94
Carbon dioxide	5.000 ± 0.015	0.05	2.50
Methane	9.000 ± 0.02	9.85	64.90
Ethane	5.000 ± 0.013	0.50	24.75
Propane	10.000 ± 0.025	0.11	19.72
Ethene	5.0000 ± 0.0015	0.10	10.06
Propene	5.0000 ± 0.0130	0.10	4.90
Hydrogen	43.0000 ± 0.0700	10.01	68.69
Carbon monoxide	9.0000 ± 0.0150	0.10	6.79

¹ The quoted expanded uncertainty is based upon a standard and certainty multiplied by a coverage factor of ($k=2$) Provide a level of confidence of approximately 95%.

² These ranges correspond to the maximum reference gas range.

Service for Prima Process Mass Spectrometers

The standard service kit ships with all Prima PRO systems and is an option with Prima BT. The kit includes all the necessary components and tools to complete routine maintenance and simplify maintenance procedures.

Rather than changing filaments or cleaning the source, users simply change the entire source, replacing it with the fully tested spare. Similarly, with the vacuum gauge, there is no need to disassemble for cleaning. Once the service has been completed, ship the kit to your nearest service center for refurbishment.



Additional resources



Peer-reviewed research

Applications of off-gas mass spectrometry in fed-batch mammalian cell culture



On-demand webinar

Real-time bioprocess monitoring of mammalian cell cultures by mass spectrometry gas analysis



Integrated software

Thermo Scientific GasWorks Process Analysis Software

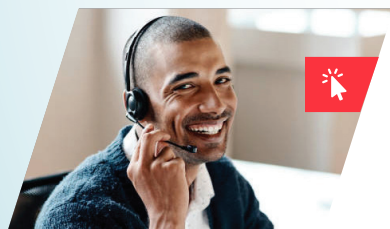


On-demand webinar

Optimize fermentation processes by implementing respiratory gas analysis PAT

About Thermo Fisher Scientific

Thermo Fisher Scientific is the world leader in serving science. Our mission is to enable our customers to make the world healthier, cleaner, and safer. We help our customers accelerate life sciences research, solve complex analytical challenges, improve patient diagnostics, deliver medicines to market and increase laboratory productivity. Through our premier brands—Thermo Scientific, Applied Biosystems, Invitrogen, Fisher Scientific, and Unity Lab Services—we offer an unmatched combination of innovative technologies, purchasing convenience and comprehensive services.



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a quote**

 Learn more at **thermofisher.com/pat**