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A Guide to Improving Biotech Processes with Mass Spectrometry Gas Analysis

ThermoFisher
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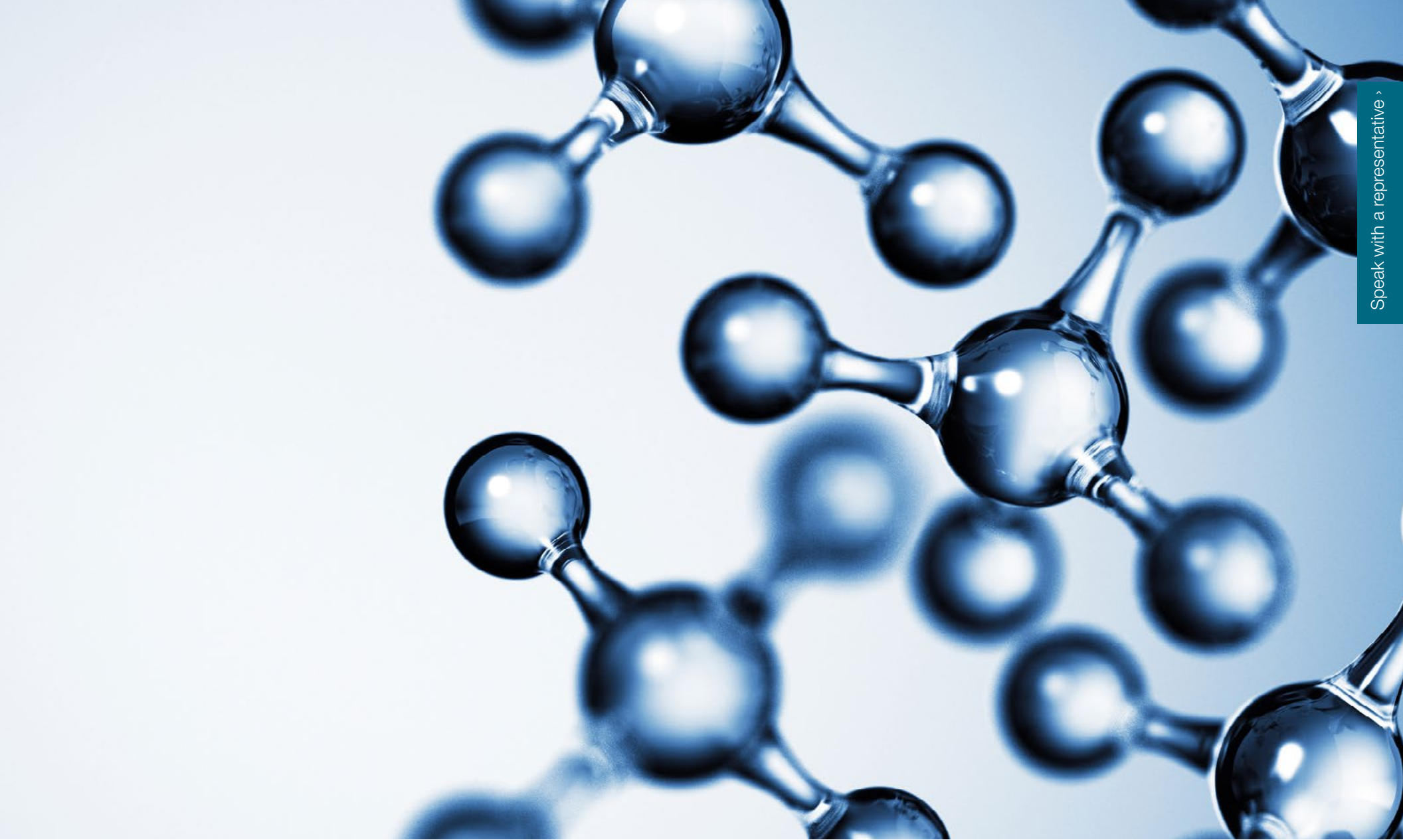
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Overview



[Thermofisher.com/PAT](https://www.thermofisher.com/PAT)

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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.

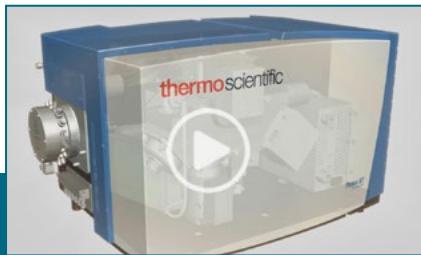
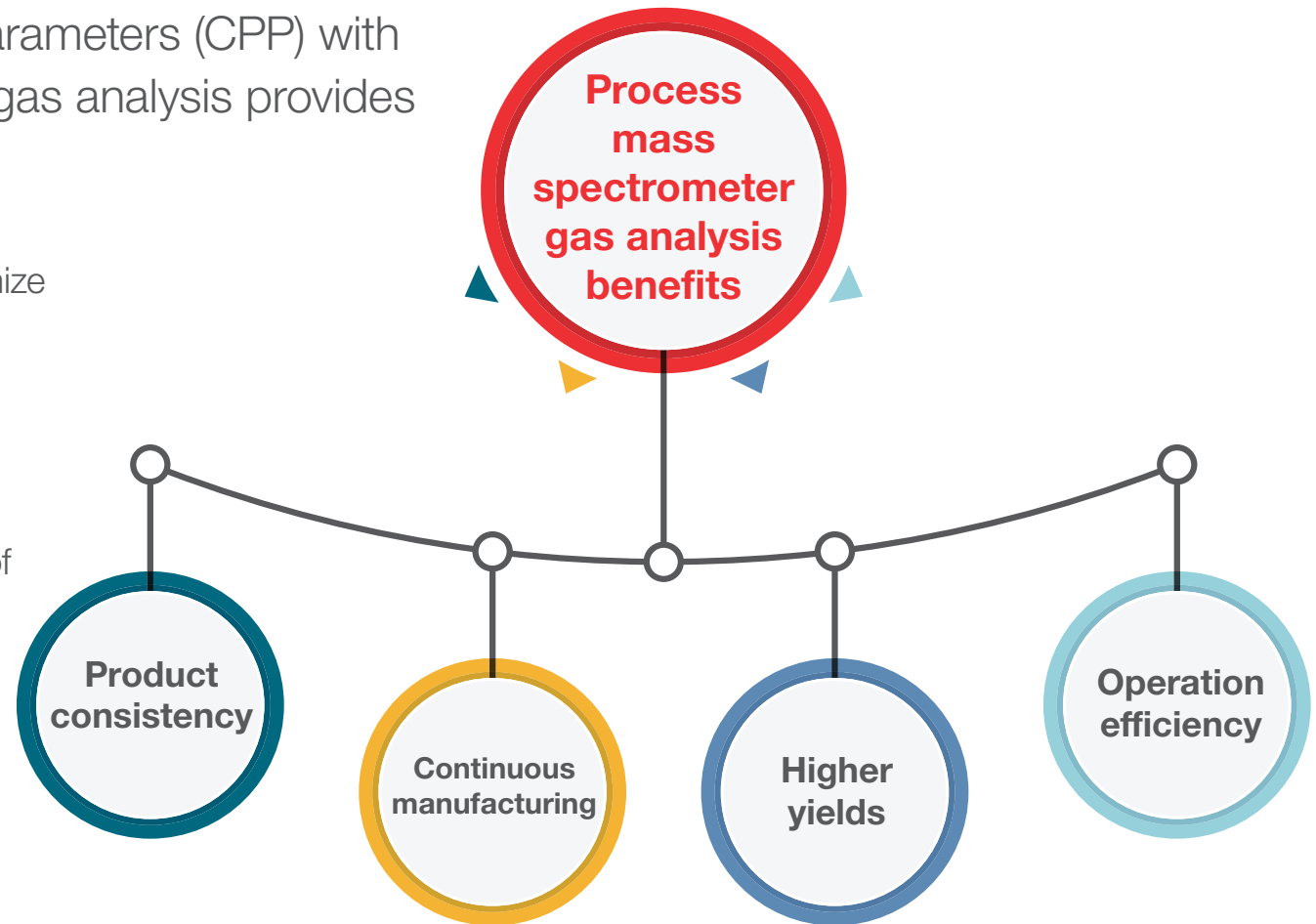


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Why gas analysis?

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



watch now to view video

[Click here](#) to watch the video Off-Gas Monitoring in Fermentations with Prima Mass Spectrometers

Process mass spectrometer gas analysis applications



Fermentation

- Prima PRO
- Prima BT
- HyPerforma Single-Use Fermentor (S.U.F)



Mammalian Cell Cultures

- Prima PRO
- Prima BT
- Hyperforma Single-Use Bioreactors (S.U.B)



Solvent Drying

- Prima PRO



Pharmaceutical Manufacturing

- Prima PRO



[Click here to view](#) Infograph: 5 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 end point for maximum product yield
- Precise measurement of Oxygen Uptake Rate (OUR), CO₂ Evolution Rate (CER) and Respiratory Quotient (RQ)

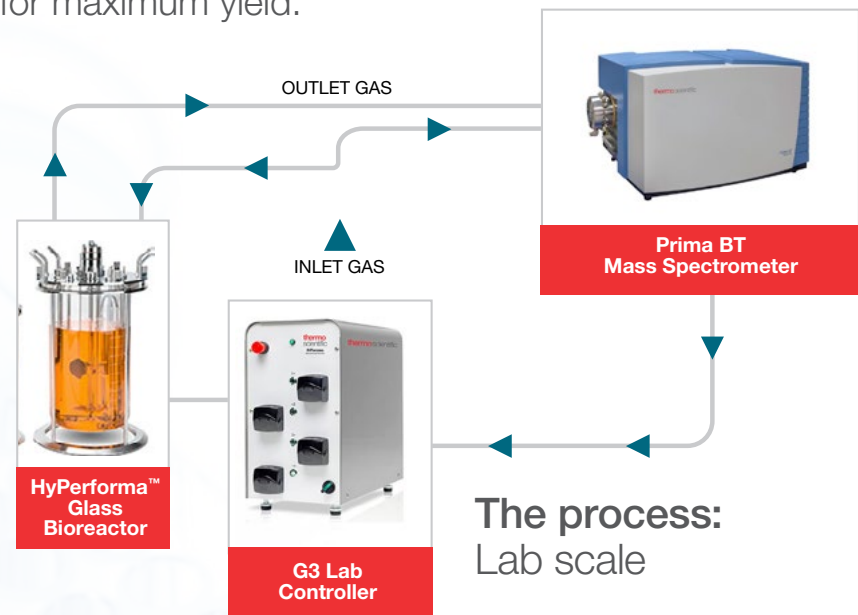
The speed of MS makes it ideal for fermentation and cell culture applications but speed must not be at the expense of precision. It is equally important that precise data is acquired; otherwise, small changes in concentration will be lost. Over 30 years of industrial experience have shown that magnetic 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 any gas analysis it is essential to monitor the state of the cell 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 mammalian cell 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 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 improve 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.

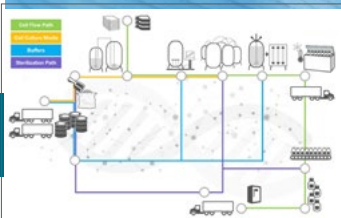


Click here to download the application note: Generating reliable quantitative solvent drying process data in the pharmaceutical industry

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 without the need for offline tests and without compromising the sterile environment. With advanced process mass spectrometers, pharmaceutical manufacturers can monitor and control multiple fermenters in real-time to ensure that each progresses according to the design of experiment and produces optimum outcomes.



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





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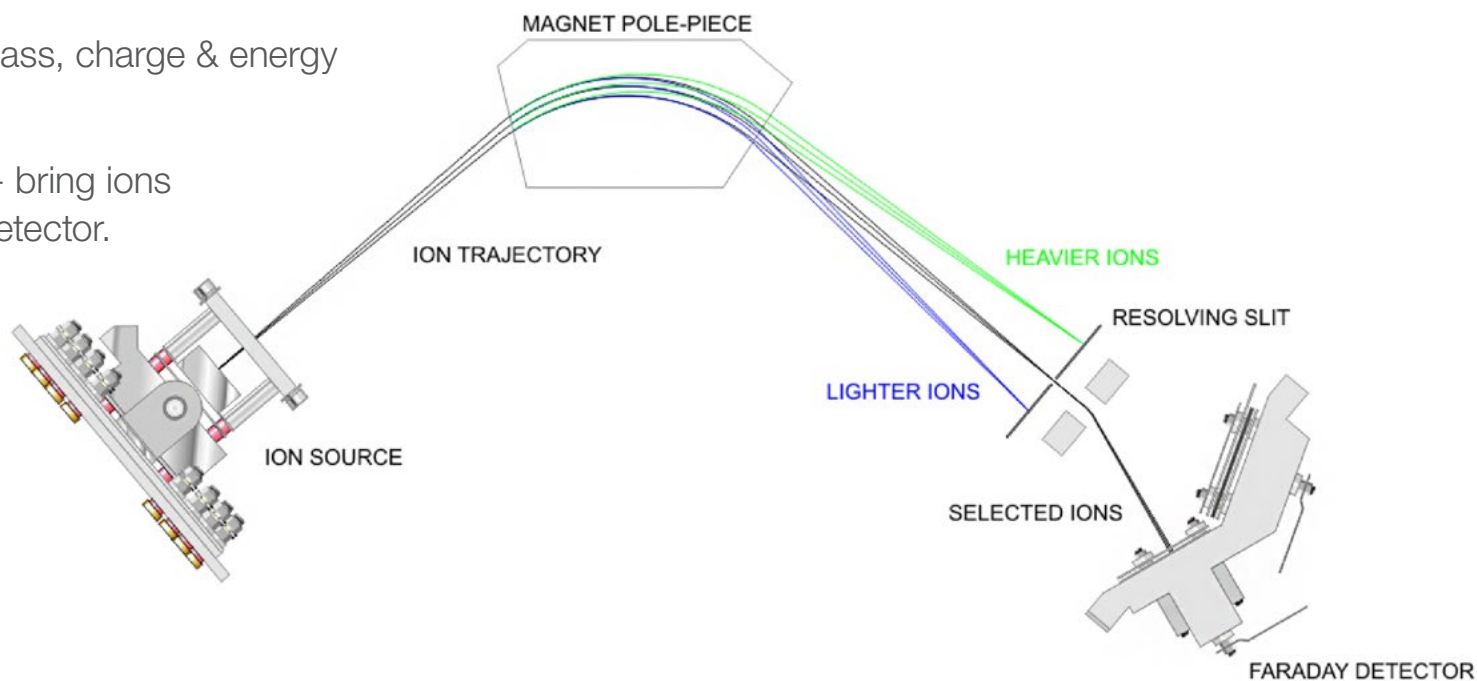
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Overview of how process mass spectrometers work

- Sample gas (here, N_2 and O_2) enters ion source and is converted to positive ions by collision with high energy electrons from filament.
- N ionized to N^+ , 28AMU, O ionized to O^+ , 32AMU. 2222
- Ions are accelerated into variable magnetic field and move in circular path.
- Radius depends on ion's mass, charge & energy and magnet field strength.
- Vary magnet field strength - bring ions sequentially onto a single detector.
- Peak height is directly proportional to concentration.
- Magnetic sector analyzer produces characteristic flat top peak—don't need to measure dead center of peak.

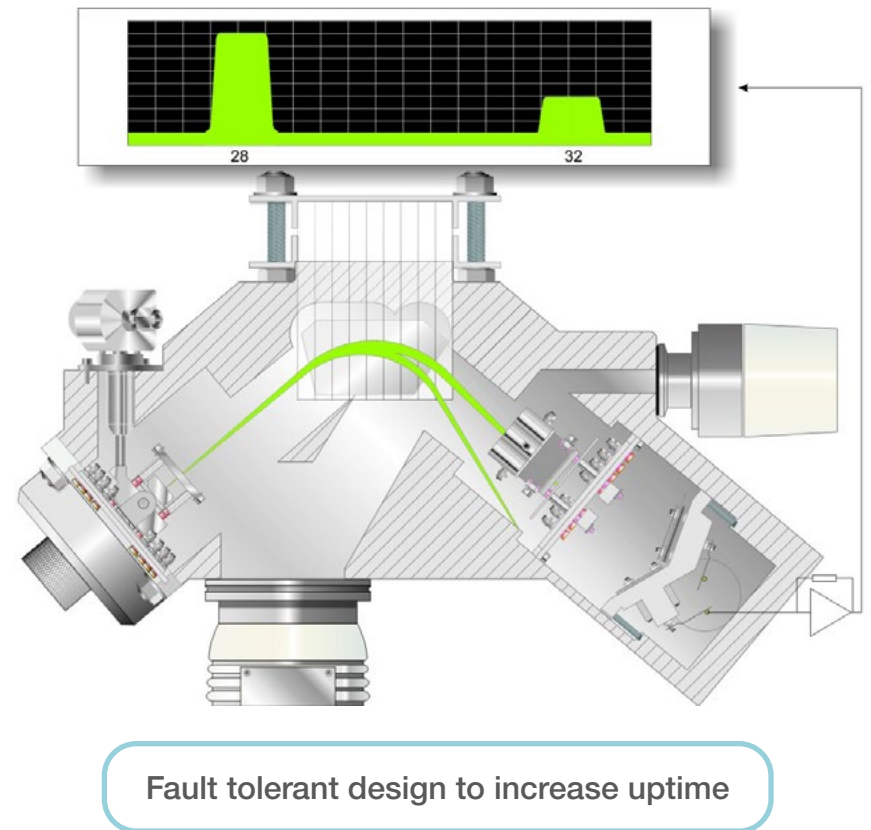


Scanning magnetic sector technology | Analog scans

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

Scanning magnetic sector technology offers precision, accuracy, long intervals between calibrations, and resistance to contamination. Typically, analytical precision is between 2 and 10 times better than a quadrupole analyzer, depending on the gases analyzed and complexity of the mixture. This resistance to contamination is essential to ensure continued operation without any requirement to interrupt the analyzer for mass filter cleaning.

The signal intensity at any specific mass position on a scanning magnetic sector analyzer appears as a flat top peak, negating the need to measure the exact middle of the peak. This means that any small drift in the mass scale will not result in a change in signal intensity.

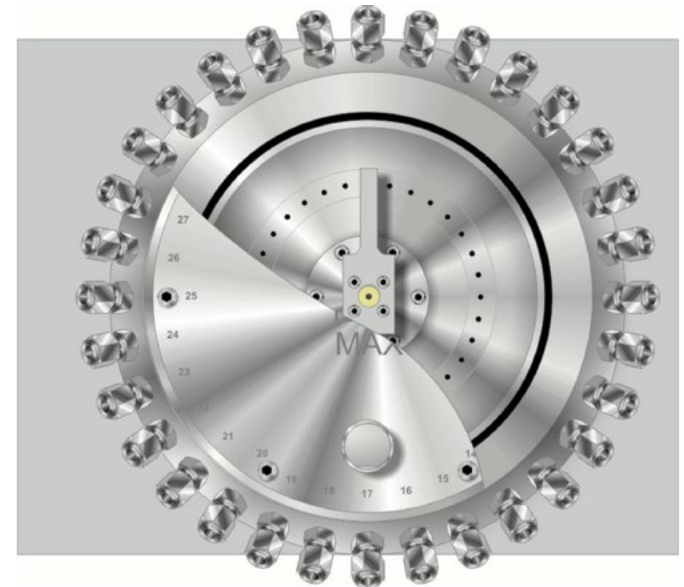


Rapid Multi-Stream (RMS) sampling | Stream status

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.

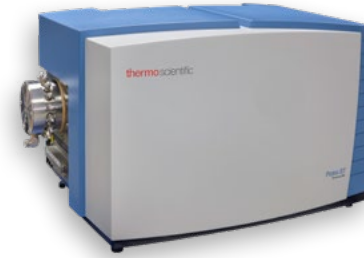
Process gas streams are one of the many analysis methods. A simple analysis of six gases has a 10 second completion time. A more advanced analysis of 40 gases has a 30 second completion time. The user has the ability to select the most efficient peak measurements for each analysis as well as the appropriate 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 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**

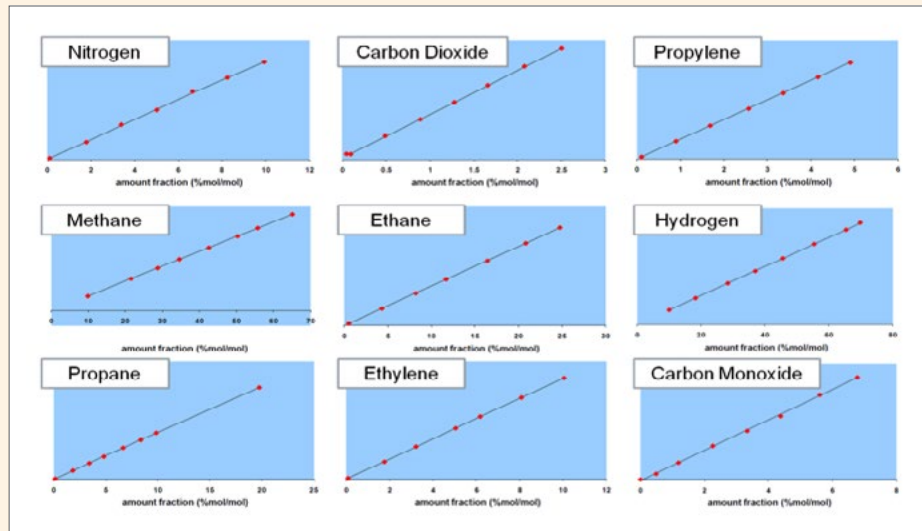


Click here to view the Process Mass Spectrometry product comparison guide

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 (%mol/mol) ¹	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 uncertainty multiplied by a coverage factor of ($k=2$) providing a level of confidence of approximately 95%

² These ranges correspond to the maximum reference gas range

Proven to have linearity superior to gas chromatography, the prima PRO scanning magnetic sector is the only process MS to be independently verified for linearity and precision by the internationally renowned and ISO accredited laboratory.



Click here to visit EffecTech website



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 components and tools necessary to complete the routine maintenance to simplify maintenance procedures.

Rather than changing filaments or cleaning the source, users now 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.



Service kit



1. Peer-Reviewed Research Paper: Application of Off-gas Mass Spectrometry in Fed-Batch Mammalian Cell Culture
2. Webinar: Real-time Bioprocess Monitoring of Mammalian Cell Cultures by Magnetic Sector Gas Analysis MS
3. Web page: GasWorks Process MS software

Additional resources



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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