

Faster market entry, higher yields, and improved quality

Real-time, inline bioprocess monitoring
and control from lab to GMP with Raman
Rxn systems & Memosens digital sensors

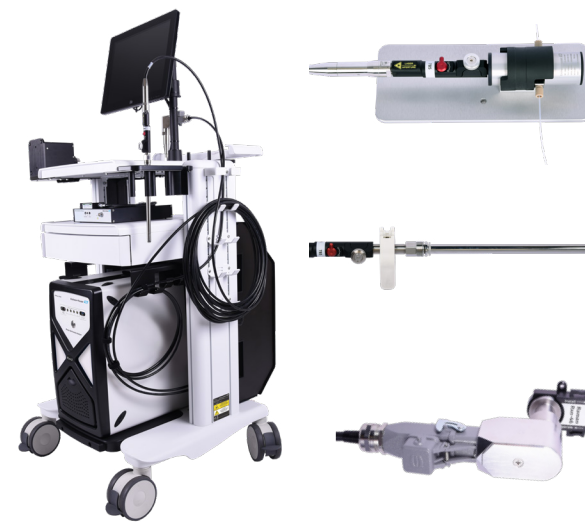


A comprehensive bioprocessing analytic portfolio

Reliable inline monitoring and control of CPPs and CQAs in real time

Endress+Hauser offers the industry's broadest analysis portfolio for lab-to-process monitoring and control of upstream and downstream bioprocessing applications.

- **Reliable measurement of bioprocess chemical and physical properties** - in cell culture, fermentation, separation and purification processes
 - Raman systems for bioprocess composition measurement
 - Memosens digital sensor technology for critical process parameters (pH, dissolved oxygen, cell growth, conductivity, and concentration)
- **Comprehensive services** - project & commissioning, support & education, maintenance, and performance optimization services (application feasibility, data modeling, FAT/SAT, IQ/OQ, and more)
- **Global support network** - direct access to Life Science process automation experts worldwide, trained specifically in cGMP



Raman Rxn systems

Full optical measurement portfolio for chemical composition analysis. Speed up process development, improve process efficiency, maximize process safety, and ensure product quality.



Memosens digital sensors

100% reliable data transmission via non-contact, corrosion-free connections. Plug & play of pre-calibrated sensors increases process uptime. Data storage in the sensor head enables predictive maintenance.

Challenges in biopharma

Product development

Bioprocesses are intricate and costly endeavors, often taking an average of 12 years to bring a product to market. In the past, traditional benchtop bioreactors required numerous manual runs to build process knowledge throughout the development cycle.

Scalability

Once a product has been proven in the lab and is ready for scale up, additional hurdles arise if equipment and technology cannot smoothly transfer to the production environment.

Process improvement

Once in production, biomanufacturers continually strive to identify and implement further process efficiency enhancements. However, this is difficult to do without adding risk and implementing extensive change management documentation.

Common bioprocess measurement issues:

- **Representative sampling** - non-representative sampling and inaccurate offline analytical methods lead to unreliable results. The sample may also change during processing.
- **Real-time transparency** - the inability to monitor bioprocesses in real time poses challenges for quality control.
- **Consistent product quality** - achieving consistent product quality remains a significant hurdle.
- **Time and expense** - re-proving analytical methods and equipment for the production environment consumes valuable time and resources.
- **Regulatory compliance** - meeting industry regulations can be difficult.

Solution

Endress+Hauser's inline, real-time bioprocessing portfolio helps scientists solve these challenges by enabling rapid knowledge buildup, optimal process performance, and seamless technology transfer from lab to commercial manufacturing.



Benefits at a glance

Unlocking bioprocess excellence

Biopharmaceutical manufacturers are increasingly seeking new ways to understand, measure, adapt, and control complex bioprocesses with accurate precision.

Inline, real-time measurement technology from Endress+Hauser provides full process transparency for better data-driven decision making along with tight process monitoring and control of crucial analytical parameters.

Our standardized analytical bioprocessing portfolio allows seamless scalability from lab to process. The ability to use identical methods and equipment during scale up ensures measurement consistency and reduces risk.

Implementing Endress+Hauser Raman and Memosens technology enables tight monitoring and control of critical process parameters (CPPs) and critical quality attributes (COAs), as well as bioprocess efficiency and easy scale up from lab to GMP.

The result? You can expect accelerated time-to-market, enhanced yield, and superior product quality, resulting in improved patient outcomes. Additionally, reduced costs and increased market share contribute to overall profitability.

All from one source

Cover all critical measurement parameters from one trusted technology partner

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24/7 process monitoring and control
Continuously monitor multiple process attributes with a single *in situ* Raman probe and digital Memosens sensors



Accurate and reliable bioprocess measurement
Assure consistent data accuracy and precision

Increased productivity and time to market
Speed processing, reduce analytical wait times, and remove bottlenecks



Total process transparency
Gain valuable process insights for better decision making, adaptability, and optimization

High plant availability
Enjoy predictive maintenance with Heartbeat Technology throughout your complete measuring points



Tight data protection
Maintain data compliance and protect against cybersecurity threats

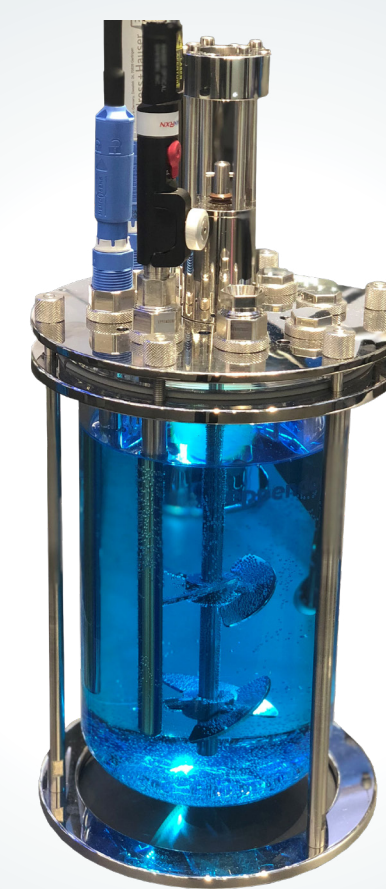
Seamless scalability
Experience smooth method, model, and technology transfer from lab to GMP manufacturing



Maximize profitability
Realize fast ROI from process automation, reduced product loss, and higher yields



Improved product quality and easier compliance
Ensure product quality and reduce regulatory burdens with better patient outcomes



Measurement technologies

An overview of the measurement principles behind our cutting-edge inline measurement systems

- **Raman spectroscopy** – measure, monitor, and control the chemical composition of your bioprocesses in real time
- **Digital Memosens technology** – precisely measure critical process parameters (pH, dissolved oxygen, cell growth, conductivity, concentration, and optical density) in real time



Raman spectroscopy

Illuminating molecular secrets

Technology overview

Raman spectroscopy, utilizing visible or near-infrared light, reveals intricate details about molecular vibrations. As light interacts with these vibrations, it undergoes inelastic scattering, resulting in a unique “molecular fingerprint.” This powerful tool enables identification, quantification, and monitoring of specific chemistries.

Role in biopharmaceuticals

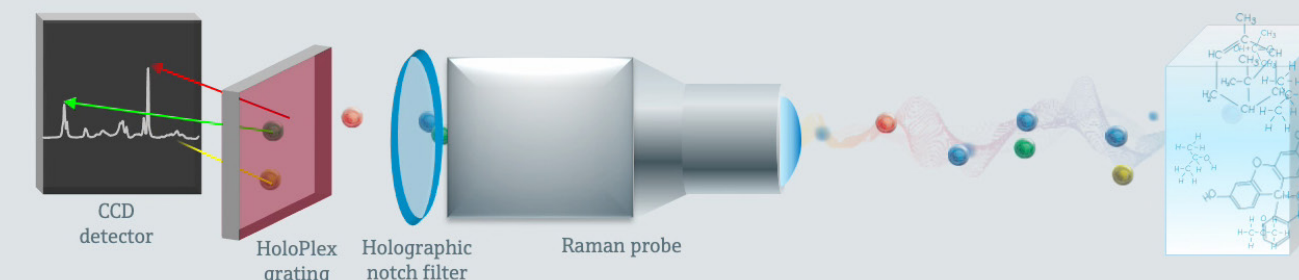
Raman spectroscopy, traditionally used in laboratory settings, has now become a crucial process analytical technology (PAT) solution in biopharmaceutical process development and commercial manufacturing.

Here’s why:

- **Real-time measurement** – Raman provides real-time, *in situ* measurements during various bioprocessing operations.
- **Insensitivity to water** – unlike other techniques, Raman measurements remain accurate even in aqueous environments, making it well suited for bioprocess applications.
- **Specificity** – Raman can distinguish between different molecules, even those with similar structures, enabling precise analysis of complex mixtures in biopharmaceutical processes.
- **Inline sampling** – directly inserted into bioreactors or flow paths, a single probe can simultaneously measure multiple parameters and quality indicators without disrupting the process.

Raman technology illustrated

- Laser light of specific wavelength interacts with molecules which causes scattering
- 1 out of 10^8 photons is frequency-shifted due to specific energy transfer (Raman shift)
- Result: specific photons allow identification and quantification of materials (solvent, products, substrate)

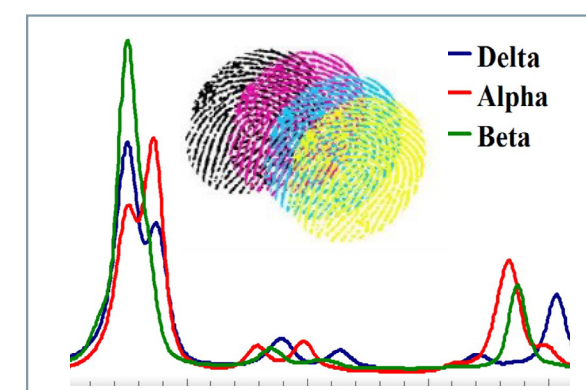


● Laser light of specific wavelength (Rayleigh scattering) ● Raman scattered light

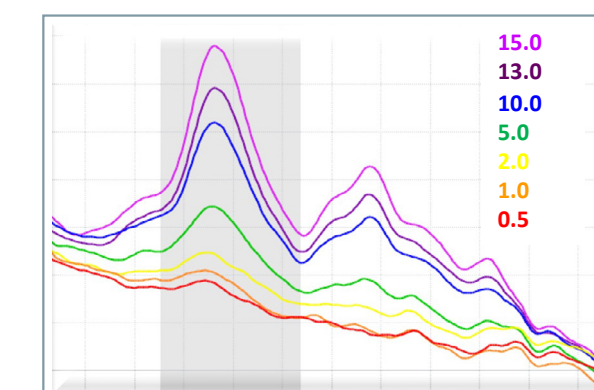
The collected light is interpreted as a spectrum by the camera, creating a “molecular fingerprint” of the material being sampled.

Raman spectra from a lab sample or process can tell us...

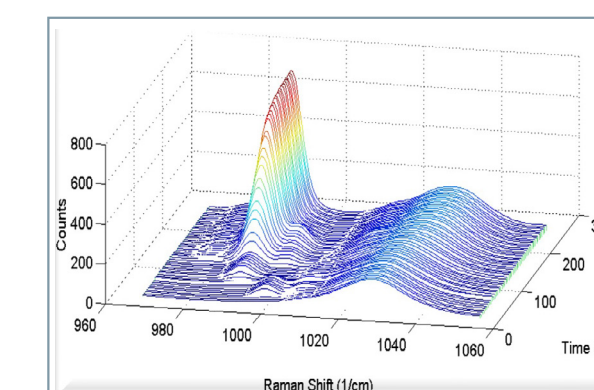
What is it?



How much?



Has it changed?



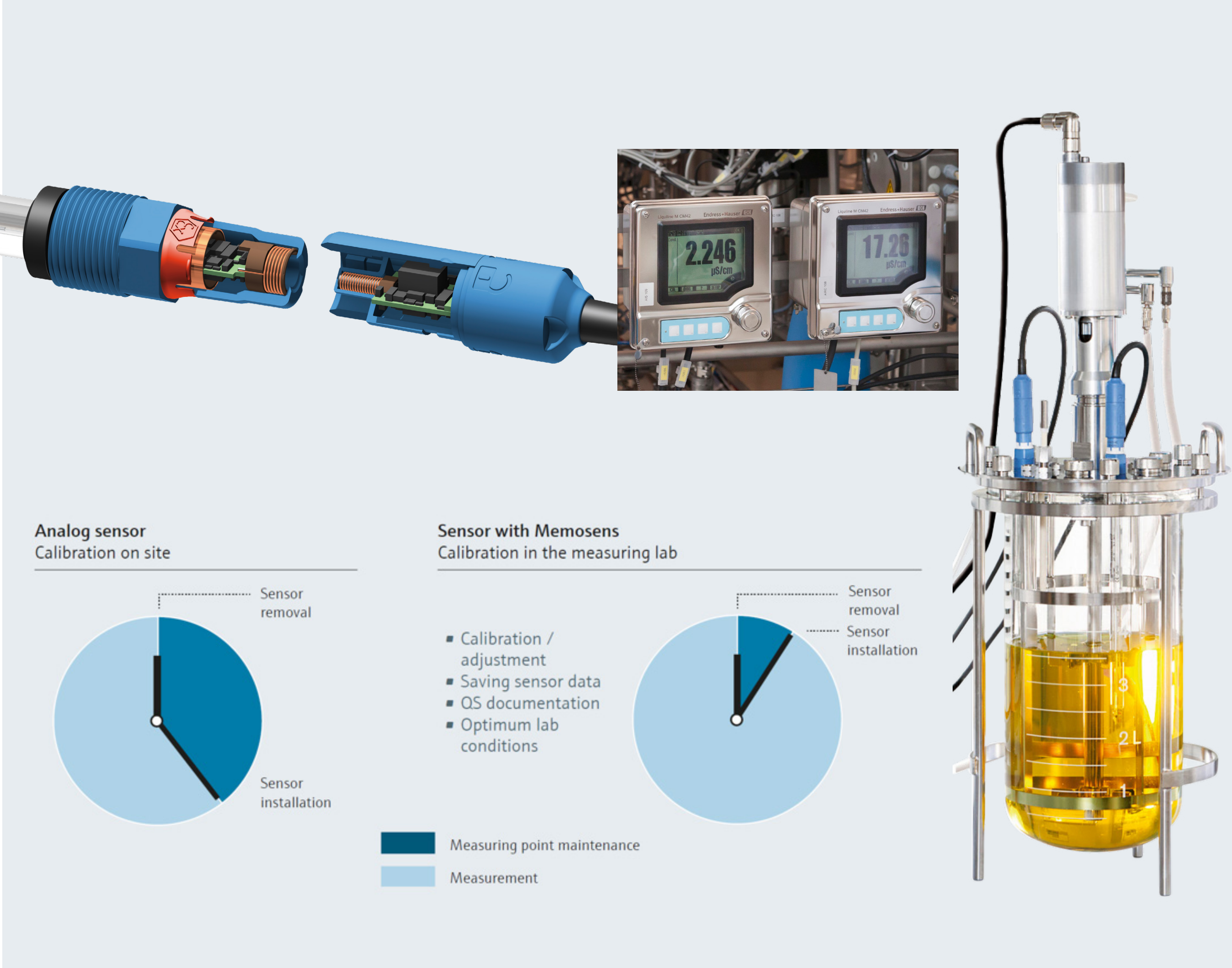


Digital Memosens technology

Simple. Safe. Connected.

Product quality, measuring accuracy and reproducibility are all critical in the highly regulated Life Sciences industry. Memosens digital technology enables you to achieve consistent measured values from the laboratory and pilot plants through to the process. With Memosens, you can perform calibration under optimum ambient conditions to ensure accuracy. Furthermore, it offers advanced diagnostic functions that provide an excellent database to decide whether a sensor is still ready for the next batch or needs to be cleaned and regenerated - a very important benefit for biotech processes.

- Maintenance strategies taken to a new level
- Very user-friendly
- Calibration performed in the comfort of the laboratory
- Safe digital data transmission during autoclaving thanks to inductive, corrosion-free sensor head and therefore 100% reliable measuring values



Analog sensor
Calibration on site

Sensor removal

Sensor installation

Sensor with Memosens
Calibration in the measuring lab

- Calibration / adjustment
- Saving sensor data
- QS documentation
- Optimum lab conditions

Sensor removal

Sensor installation

Measuring point maintenance

Measurement



Applications in biopharma

Solutions designed to meet upstream and downstream requirements

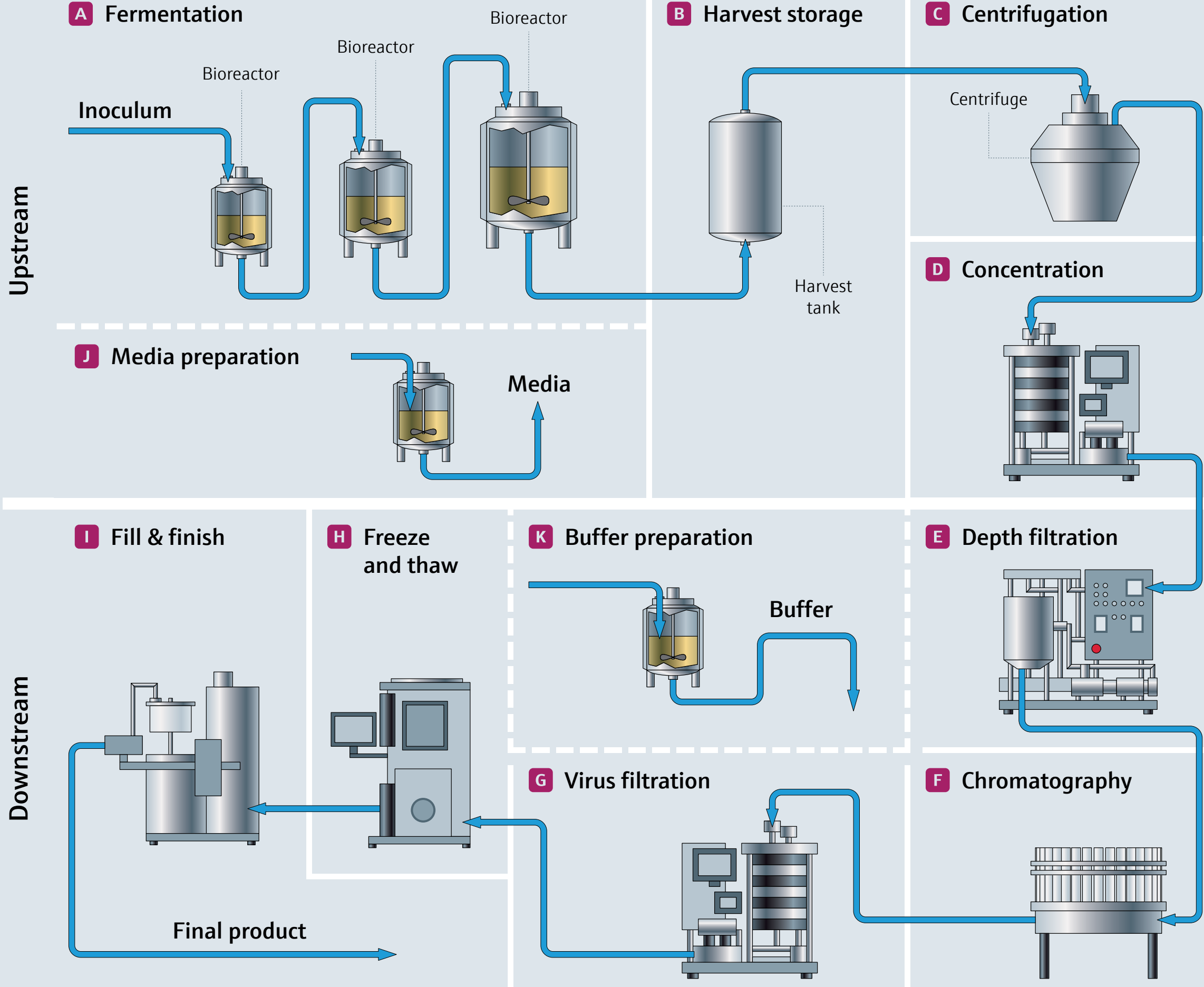
In the dynamic world of bioprocessing, precision and control are paramount. Endress+Hauser is at the forefront of transforming this space with innovative inline process measurement systems. We empower organizations to measure CPPs and COAs in real time, maximizing quality and efficiency throughout upstream and downstream processes from cell cultivation or fermentation to the final product.

Real-time insights - our systems offer immediate feedback on key process variables, eliminating the delays associated with offline methods.

[Click to go to upstream applications](#)

[Click to go to downstream applications](#)

Bioprocess overview



Overview of fermentation process steps in bioprocessing with opportunities for inline analysis



Upstream applications

Cell cultivation and fermentation

In the critical upstream biomanufacturing phase, scientists seek to produce the target molecule. Bacteria, fungi spores, and mammalian cells multiply during cell cultivation and fermentation processes, with bioreactors playing a central role. Precise adjustments of chemical and physical parameters – such as composition, pH value, and oxygen concentration – are crucial for cell growth. Having the best-suited cell lines and culture media that minimize impurities and generate the correct product efficiently is important to improve process outcomes.

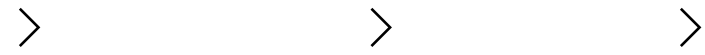
Solution

Real-time, inline analysis is an indispensable tool for upstream process optimization. Scientists rely on Endress+Hauser's Raman systems and Memosens digital sensors to measure chemical composition and essential process parameters reliably. With 24/7 process monitoring and control, they can optimize bioreactor conditions and feed control, ensuring optimal growth for microorganisms and cell cultures.



Upstream bioprocessing (USP)

Our solutions are engineered to provide real-time data on the chemical composition and physical properties of your bioprocesses directly from the bioreactor to seamlessly monitor key process attributes like cell density (TCD, VCD), glucose levels, lactate concentrations, amino acids levels, pH, DO, concentration, and more.



Robust chemical composition measurement in USP

Harness the power of Raman to measure glucose, lactate, amino acids, cell density, titer, & more

In the upstream realm, Endress+Hauser Raman systems shine, revealing molecular composition process insights that could not be “seen” before. Upstream applications well suited to Raman measurement include:

- Metabolite monitoring
- Feed control
- Cell growth
- Monitor capsid integrity and filling
- Yield predictability
- Compliance with regulatory standards
- Many other PAT/QbD applications

Reusable or single-use versatility

Our Raman systems offer the utmost flexibility for a variety of bioreactor setups. Single-use Raman systems, such as our bio multi optic and sleeve offering, are designed to be used for one or several batches before being replaced. This eliminates the need for additional cleaning, sterilization and component validation. It also provides opportunities for reduced material use, costs, cross-contamination risks, and manufacturing times.

Products for chemical composition measurement in USP

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Precise process parameter measurements in USP

Your liquid analysis measuring point with Memosens

Memosens digital sensors capture pH, DO, and cell growth parameters. Paired with a transmitter from the Liquiline platform and the matching assembly, continuous monitoring is easier than ever.

- Safe digital data transmission: inductive, corrosion-free, 100% reliable
- Sensors store up to 8 times more calibration data for predictive maintenance and IIoT services
- Fast plug & play with pre-calibrated sensors
- International de-facto standard

Select products for monitoring pH, DO, conductivity, turbidity, and concentration in USP



Downstream applications

Separation and purification process analysis

In the downstream phase of bioprocessing, the target molecule is isolated from the reaction mixture and purified. Maintaining product quality through each step is paramount.

Downstream operations encompass processes such as:

- Fill and finish
- Free and thaw
- Buffer preparation
- Depth filtration
- Virus filtration
- Chromatography
- Final product

While upstream applications have seen widespread adoption of PAT solutions, downstream unit operations face unique challenges.

Common downstream analysis challenges

- Reliance on off-line analysis techniques
- Slow response times
- Insufficient nominal ranges
- Background interference
- Accuracy issues
- Lack of stability
- Lack of quality attribute specificity

The increasing complexity of purification steps due to intensified upstream processes has also highlighted the need for innovative solutions in downstream bioprocessing.

Solution

Endress+Hauser offers tailored Raman systems and Memosens digital sensors which combine practical techniques with precision analysis to enable scientists to formulate biologics for safe and effective patient outcomes.



Downstream bioprocessing (DSP)

Precisely measure critical parameters like composition, pH, dissolved oxygen levels, conductivity, and concentration rates in real time. Ensure target protein quality while monitoring aggregates effectively.

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Robust chemical composition measurement in DSP

Employing Raman for precise high-speed, low volume sample measurement

Raman spectroscopy is increasingly playing a crucial role in downstream chemical composition analysis. Endress+Hauser's Raman flow assembly was designed to fill that market need, bringing process insights and control to downstream bioprocessing unit operations.

The Raman flow assembly is comprised of a micro flow cell and associated micro flow bench. The flow bench provides flexibility to swap out flow cells any time without impacting the process or sterility. The system easily connects to an Rxn-10 probe paired with a Raman Rxn embedded analyzer.

Together, the Raman flow assembly system meets the speed demands of downstream by optimizing Raman collection for low-turbidity, low volume samples. It achieves lower limits of detection through enhancement of the Raman signal.

Ideally suited for development-scale flow rates, this system provides real-time monitoring, rapid process optimization, and process control for chromatography and other downstream unit operations, including:

- Aggregation
- Protein crystallization
- Formula stability
- Product CQA
- Protein concentration
- Buffer excipients
- Midstream analyte monitoring in permeate

Chemical composition measurement in DSP

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Precise process parameter measurement in DSP

Memosens digital sensors and process photometers for precise, stable measurements of downstream process measuring points

Memosens makes every sensor digital with integrated memory

- Simple sensor exchange with pre-calibrated sensors
- No calibration in the field necessary; high-quality calibration in the laboratory
- Active communication: alarm signal when no connection between sensor and transmitter

Process photometers with precise and reliable measurement and traceable in-line calibration with EasyCal™. Benefit from low maintenance and no need for consumables.

Select products for monitoring pH, DO, conductivity and concentration in DSP



Our product differentiators

Most complete and state-of-the-art bioprocess measurement portfolio

- **Broad measurement offering** – for a wide range of parameters (composition, cell viability, pH, DO, cell growth, concentration, conductivity, & more) for upstream and downstream applications
- **Scalability and versatility** – our standardized instrumentation is designed to scale seamlessly from lab to process, micro to GMP manufacturing, and benchtop to stainless steel or single use
- **Unsurpassed model transferability** – Raman analyzer and probe standardization through simple-to-use calibration and verification kits offer unparalleled chemometric model transferability
- **Automation & digitalization** – our Raman platform features OPC, Modbus, and https automation capabilities while our Memosens digital sensors, in combination with the Liquiline platform, features Heartbeat Technology, ProfiNet, Modbus, Ethernet IP, Webserver & many more
- **Stable and reliable measuring values** – accurate and consistent measurements from lab to manufacturing, even after CIP/SIP/ autoclaving
- **Fast response time** – inline measurements taken in real time for near instantaneous results
- **Superior designs**
 - Raman multi-channel capabilities with high-quality probe windows, optimized for bioprocessing
 - Memosens plug & play digital sensors known for simple, safe inductive non-contact connections, reduced noise, and long lifecycles





Why partner with Endress+Hauser?

30+ years of Life Sciences innovation and customer success

One source, infinite precision

Imagine a world where all your crucial bioprocess parameters are measured and analyzed by one reliable source, bringing efficiency and precision right to your fingertips. Your search ends with Endress+Hauser. We do not just offer instrumentation; we provide solutions that meet your unique application needs, optimized for your installation environment.

Unparalleled expertise

For over three decades, we have partnered with Life Sciences companies to empower them to automate and optimize their bioprocesses. Our collaboration with industry leaders in both Raman and Memosens technology has honed our expertise, making us the most trusted ally in the biopharmaceutical analysis arena.

Tailored innovation

Our complete bioprocessing portfolio - including Raman analyzers, probes, and optics as well as liquid analysis digital sensors and transmitters - is engineered to meet the rigorous demands of the biopharmaceutical landscape.

Seamless scalability

Using standardized instrumentation ensures that your product's transition from lab discovery to commercial manufacturing will go smoothly. Our hardware and software were designed for lab to process – meaning all models, methods, and technology can scale easily without measurement inconsistency or quality risk.

Global support, local excellence

Endress+Hauser offerings come with the reassurance of decades of proven performance in the field. Our reliable world-class devices are also backed by a global network of Life Sciences service and support experts trained in GMP.



People for Process Automation



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