Raman flow assembly Precise composition measurement of high-speed, low-volume samples in downstream bioprocessing



Endress+Hauser Rxn-10 probe connected to a Raman flow assembly

The latest innovation in our Raman probe accessory portfolio – the Endress+Hauser Raman flow assembly – brings in-line Raman spectroscopy measurement to downstream unit operations in bioprocessing. This highly adaptable, *in situ* downstream sample interrogation system integrates directly into process streams, reducing the need for off-line measurements. The Raman flow assembly enables enhanced signal generation while accurately monitoring material in a flow path. Components include:

- A reusable optic (micro flow bench) connected to an Rxn-10 probe, which has no product contact and is tuned for specific flow cell and sample conditions, and
- A micro flow cell which interfaces with the micro flow bench and allows the sample to flow within it. The micro flow cell may be sterilized by approved methods and can be either reused or discarded after use.

Fast downstream bioprocess composition measurement

The Raman flow assembly is a process analytical technology (PAT) that accommodates the reduced volumes and shorter cycle times commonly seen in downstream process development. In contrast to upstream bioprocessing applications where processes evolve slowly, composition changes happen rapidly in downstream. The Raman flow assembly meets these speed demands by optimizing Raman collection for low-turbidity, low volume samples. Ideally suited for development-scale flow rates, the Raman flow assembly provides real-time monitoring, rapid process optimization, and process control for chromatography and other downstream unit operations.



Benefits at a glance

- Brings Raman-based process insights and control to downstream bioprocessing unit operations
- Achieves lower limits of detection through enhancement of the Raman signal
- Provides continuous, realtime measurements with high sensitivity for development-scale flow rates
- Easily connects to an Rxn-10 probe paired with a Raman Rxn embedded analyzer, and ensures transferability when used with the Raman flow assembly calibration and verification kit
- With the micro flow bench, provides flexibility to swap out flow cells any time without impacting your process or sterility

People for Process Automation



Raman micro flow bench

Micro flow bench overview

- Provides a secure interface for the micro flow cell and serves as the non-wetted portion of the Raman flow assembly
- Delivered ready to connect to the Rxn-10 probe in benchtop position (other mounting options available)
- Designed for perfusion and downstream applications to allow liquid material to be analyzed without interrupting the flow
- Features an amplification option which delivers 3-4 times signal improvement over traditional immersion optics in non-turbid material¹
- Leverages the internal geometries of the micro flow cell to enhance the total signal-to-noise, allowing for faster sampling time or lower limit of detection (LOD)
- Comes standard with an amplifier to enhance the Raman signal
- Arrives factory tuned for the unique micro flow cell and application based on the fluid-path thickness and/or the refractive index of the sample

¹System-specific variables ultimately determine the level of enhancement

Configurable options for the micro flow bench include:

- A fixed beam dump that safely blocks the amplified signal to collect spectra in back-scatter mode only, which is useful for calibration/verification events, as well as for running experiments which do not require the signal enhancement from the amplifier
- OEM-integration with customizable mounting options if a solution other than the benchtop version is preferable

Micro flow cell overview

- Serves as the wetted portion of the Raman flow assembly, compatible with the flow bench
- Features a sealed, fixed focus design with no movable parts for long-term measurement stability and superior signal performance
- Integrates directly into applications where static samples are not preferred for either integration and process parameters, or where sample changes occur (such as fluorescence decay or heating)
- Designed to produce laminar flow within a wide range of volumetric flowrates, pressures, tubing diameters, and fitting options
- Comes standard as ASME BPE SF4 Bio-Compatible, and may be cleaned and sterilized for re-use or discarded after each use



Raman micro flow cell

How to use the Raman flow assembly

Raman flow assembly components can be quickly configured using an easy modular design.

- The Rxn-10 probe slides easily onto the micro flow bench
- After pulling back and twisting the light shield, the micro flow cell can be placed into the center cavity of the micro flow bench
- Once the micro flow cell is in place, the light shield should be returned to the closed position to secure the micro flow cell and offer added safety to the user

The system has been designed to ensure maximum transferability, so replacing the micro flow cell on the micro flow bench will not affect the integrity of the resulting spectrum.



Connecting the Rxn-10 probe and the micro flow bench



Inserting the micro flow cell into the micro flow bench



Quick and easy calibration and verification

A specially designed Raman flow assembly calibration and verification kit is available for this product. It contains everything needed to standardize your Raman system for lab-to-process scalability. Requiring no external power, these tools boost efficiency and reduce downtime via easy field deployment. The kit contains non-wetted parts which offers flexibility to be used any time without impacting sterilization.

Technical specifications ²		
	Micro flow bench	Micro flow cell
Field of application	For use in downstream (aggregation, protein crystallization, formula stability, product COA, protein concentration, buffer excipients) and midstream (analyte monitoring in permeate) applications	
Sampling probe compatibility	Rxn-10 probe	Rxn-10 probe
Laser wavelength	785 nm	785 nm
Sample interface	Temperature (operating): O to 40 °C (32 to 104 °F) Temperature (storage): -10 to 50 °C (14 to 122 °F)	Temperature (operating): O to 40 °C (32 to 104 °F) Temperature (storage): -20 to 60 °C (-4 to 140 °F) Maximum pressure: 4.8 barg (70 psig) Relative humidity: <90 % non-condensing
Wetted materials	n/a	Body: 316 stainless steel Surface finish: Ra 15 with Electropolish to ASME BPE SF4 finish Adhesive: USP Class VI and ISO 10993 compatible Window: Proprietary material, optimized for bioprocesses
Process connection	n/a	5/16-24 flat bottom ferrules; up to 3/16 inch OD tubing
Fluid path thickness	1.0 to 5.0 mm (flow cell driven)	2.5 mm
Flow conditions / maximum volumetric flow rate	n/a	50 mL / min for laminar flow, 100 mL / min max
Dimensions (width x height x depth)	254 x 102 x 66 mm (10.0 x 4.0 x 2.6 in)	46 x 25 x 11 mm (1.8 x 1.0 x 0.4 in)
Cleaning & sterilization	n/a	CIP, SIP
Calibration method	Micro flow bench calibration cell	n/a
Verification method	Micro flow bench verification cell with 70 % IPA	n/a

²For complete product specifications, please refer to the Technical Information (TI) manual for the Raman flow assembly or go to <u>www.endress.com</u>.

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