



## **QIC-Biostream**

### **Exhaust gas analysis of small scale fermenters**

#### **Summary**

The application of the Hiden QIC-Biostream gas analysis system is to monitor the off-gas and vapours from up to 80 small scale fermenters for yield optimisation and process screening.

#### **Introduction**

Biotechnology is an extremely important area for the 21<sup>st</sup> century and information relating to yield of a product is crucial to most Biotech Companies.

From a research perspective, it is very useful to effectively monitor the yield from small scale fermenters to prove the worth of a particular product before scaling up production to large scale plants.

The QIC-Biostream provides accurate fast, real time measurement of exhaust gases from the small gas sample available from small scale fermenters.

The Hiden QIC-Biostream is a mass spectrometer gas analyser configured with a Proteus 40 way multistream sampling valve configured for low flows from 4ml/min, making it an ideal instrument for measuring fermenter off gases and vapours with high accuracy.

## QIC-Biostream

### Overview

In a conventional multi-stream sampling system small diameter sample tubing is used to connect the sampling point to the multi-stream selection device which selects individual streams for analysis. Sample gas flow through the sample tubing is induced by creating a pressure gradient along the tube. This gradient may be achieved by running the sample source at a positive pressure & venting the sample flow to ambient pressure after analysis. Alternatively, a sampling pump may be connected to the analyzer exhaust if it is not possible to pressurize the sample source. Sample transit time from the sampling point to the analyzer is very dependent on the sample flow rate & the construction of the multi-stream selection device. This type of system will typically accept individual sample flow rates from several litres/minute down to 0.1 litres/minute. Sample transit times usually become unacceptably long (several minutes) below 0.02 litres/minute.

Typical low flow applications are:-

- (a) Exhaust gas analysis of fermentation micro-reactors where the small scale requires minimal flow rates.
- (b) Mammalian cell culture where the slow growth rates/low specific metabolic rates of the cultures require low gaseous flow rates to provide continuous determination of oxygen uptake & carbon di-oxide production rates.
- (c) Spatially resolved mass spectrometry (SPACI ms) for low-intrusion monitoring of composition gradients within gas streams.

### Description

The schematic on the following page depicts the low-flow configuration.

The system utilizes the unique capability of the Proteus multistream selector valve to operate under very low pressure (vacuum) conditions.

This system is optimized for fast response with very low sample flow rates. This is achieved by replacing the sample lines with small-bore capillary tubing. The sampling lines then become the 1<sup>st</sup> stage of the inlet pressure reduction system. The exhaust of the Proteus valve is connected to the dry scroll pump P2 to provide a vacuum of a few mbars absolute within the valve. Pirani gauge G2 is provided for monitoring this pressure, mainly for diagnostic purposes.

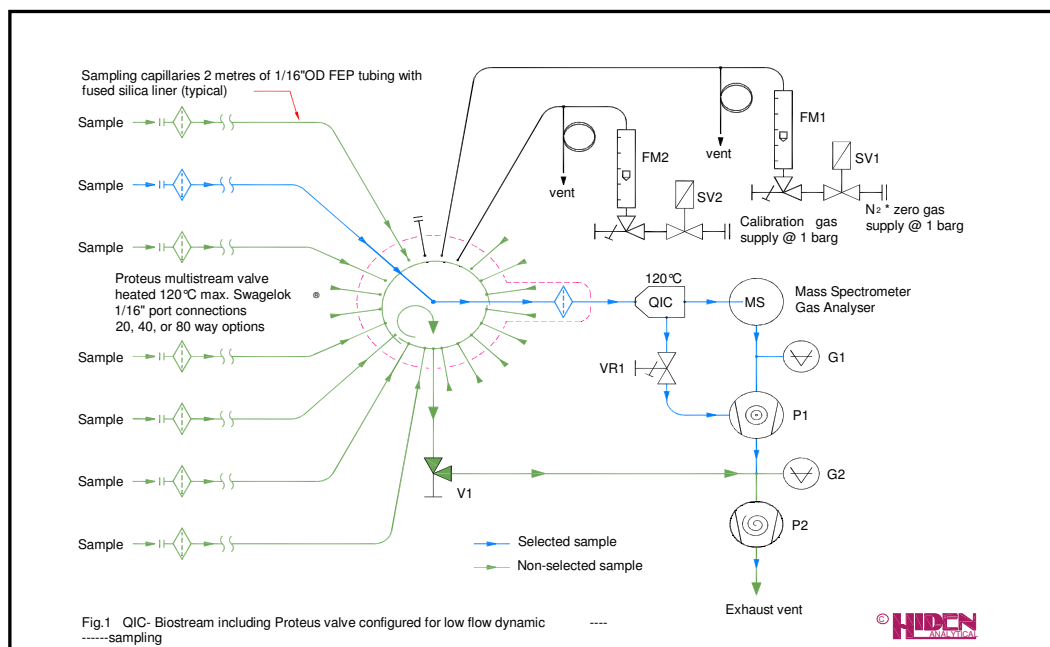
Atmospheric pressure sample gas enters the capillary sample tubing at the sampling point at 1.8 metres/sec (typical for 0.2mm ID x 2.0 metre sampling capillary) then accelerates rapidly along the tubing due to the progressive expansion of the sample. By the time the sample arrives at the Proteus valve its pressure has reduced by a factor of >200 & hence its volume flow increased by a factor >200.

For example, 4 ml/minute atmospheric flow expands to  $4 \times >200 = 800$  ml/min (0.8 litres/minute)

This increase in sample volume flow rate provides rapid sample transit along the sampling capillary & the fast switching response through the Proteus valve. Selected sample flows from the Proteus valve directly to the 2<sup>nd</sup> reduction stage. This 2<sup>nd</sup> reduction stage is a variant of the Hiden QIC inlet with the normal QIC capillary connection port coupled directly to the outlet of the Proteus valve. The QIC sample bypass flow is pumped via the inter-stage port on turbomolecular pump P1.

The mass spectrometer housing is also a special type to optimize pumping at the ion source for rapid sample removal for low sample memory effects.

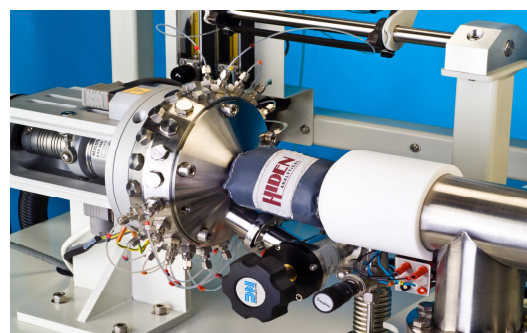
## Schematic of system



## QIC Biostream system



QIC-Biostream



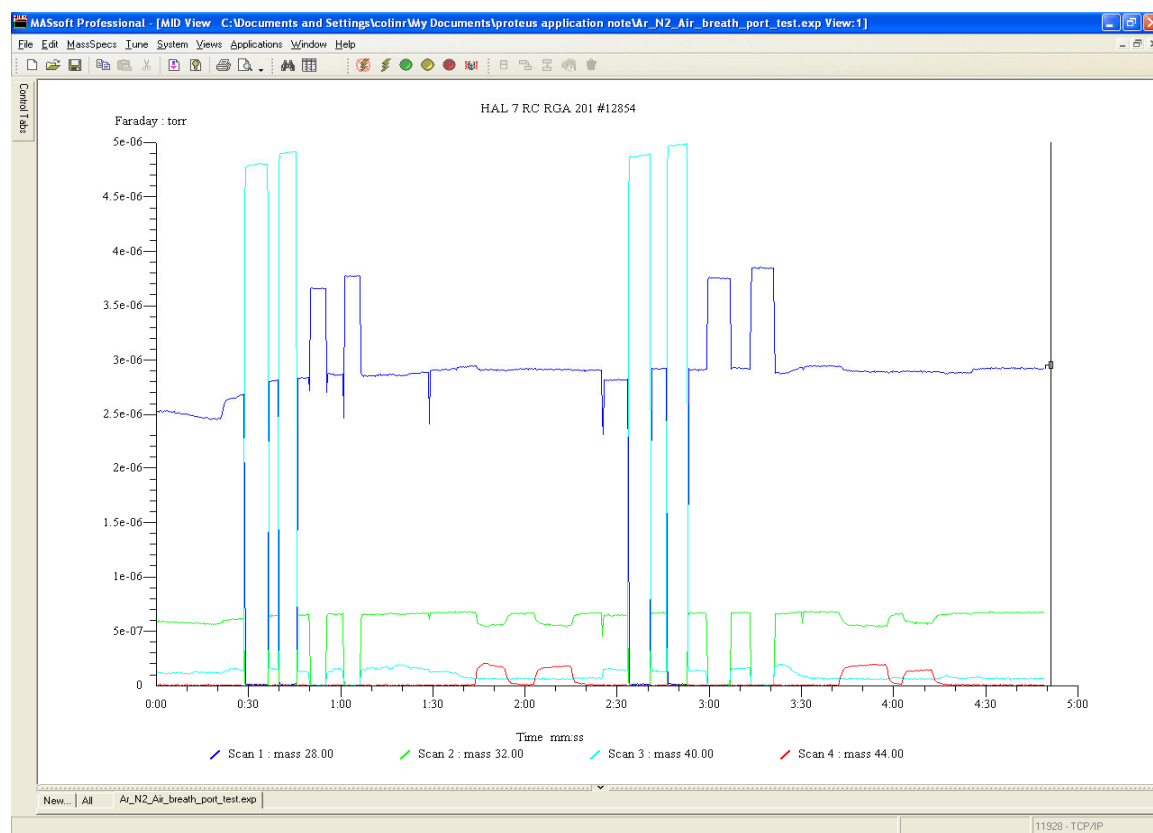
Low flow 40 way proteus multistream sampling valve

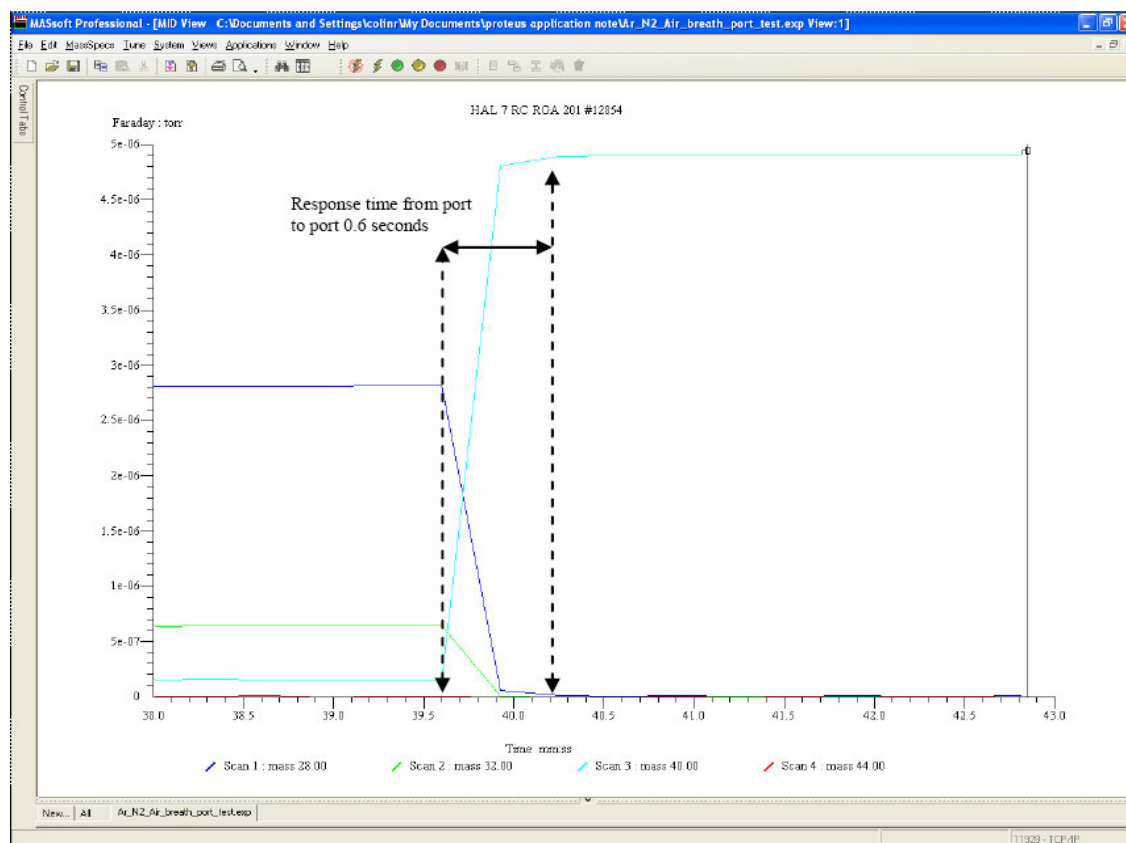


Sampling lines, female luer lock fittings, shown with disposable hydrophobic filters

## Data

Shown below is data from the QIC-Biostream. This data illustrates the systems fast response switching between sample lines.





The switching time between sample streams is as low as 0.6 seconds. The rapid switching time provides real time analysis from multiple small scale fermenters with fast, accurate repeatable data and with no memory effects from the previous ports.

### Conclusion

The information obtained from the QIC-Biostream instrument provides the user with crucial and accurate information as to the yield characteristics of all the monitored fermentation processes in a single experiment.

This data provides conclusive information as to whether a specific process is useful to scale up for large scale production.

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