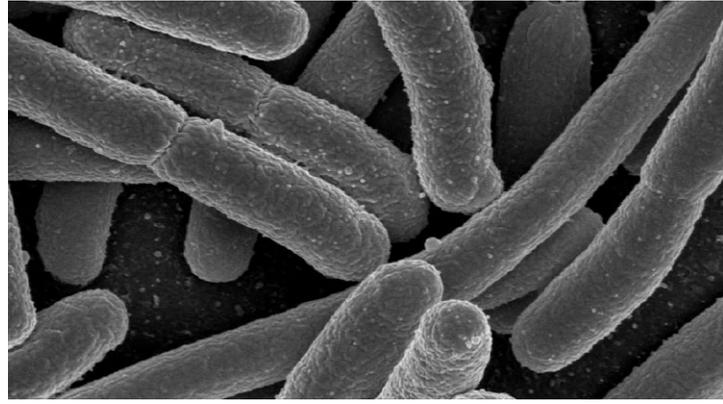




Applications



> Bioprocess Monitoring:

Trace Gas VOC Monitoring Analysis of Fermenter Off-Gas

THE CHALLENGE IN THE BIOTECH INDUSTRY

Modern biopharmaceutical drugs are produced in biotechnological fermentation processes.

The monitoring of these processes is becoming increasingly relevant, especially in the manufacturing sector, to promote cost-effective production. To date, biotechnical processes are generally monitored using off-line analysis, which is labor and cost intensive, providing results often too late for corrective actions.

THE SOLUTION

IONICON PTR-MS can provide highly relevant process information on-line and in real-time.

PTR-MS systems monitor a large spectrum of volatile metabolites in the off-gas of fermenters. The measured concentrations are directly linked to the activity of microorganisms and can thus be used for on-line quality assurance. Such an approach is in-line with the Process Analytical Technology (PAT) initiative being recommended by the US Food and Drugs Administration (FDA) to improve quality, safety and efficiency in drug manufacturing processes.

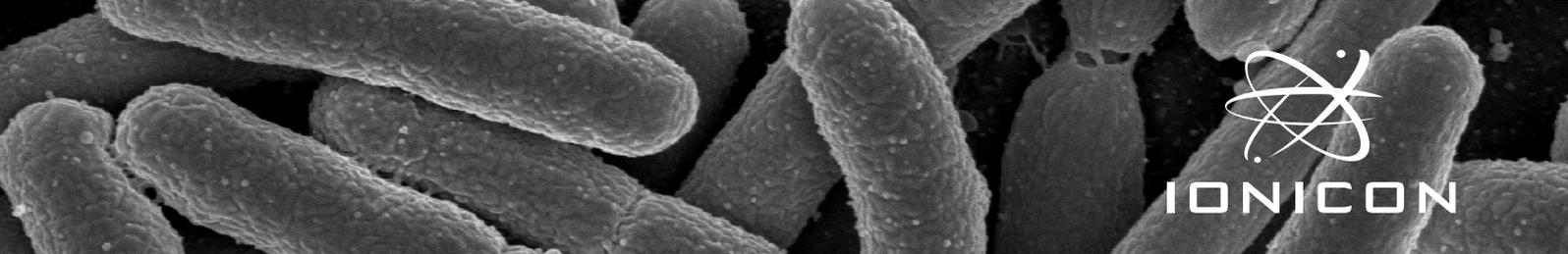
This non-invasive implementation has been tested in industrial, Good Manufacturing Practice (GMP) controlled environments.

PTR-MS

- > Process monitoring and control
- > Real-time analysis of volatile metabolites
- > Multiple sampling points monitoring
- > Suitable for GMP controlled production

Find out more:

www.ionicon.com/biotech



Scanning electron micrograph of Escherichia coli. Credit: Rocky Mountain Laboratories, NIAID, NIH.

ONLINE MONITORING IN THE BIOPHARMACEUTICAL INDUSTRY

In a bioreactor, volatile organic compounds (VOCs) are emitted as metabolic by-products of microbial growth and production. Real-time monitoring of these volatile metabolites in the off-gas of a bioreactor using PTR-MS allows gauging the activity of microorganisms for quality assurance and process control. In E. Coli fermentations we observe up to 70 VOCs with notable concentrations and distinct variations over time - prominent examples are shown in figure 1.

PROCESS MONITORING - PTR-MS SETUP

Of central importance in this context is a fast and quantitative transfer of the sample gas to the PTR-MS. IONICON has developed an optimized coupling system for biotech applications (see figure 2) which provides dilution of the sample gas, safety measures, multiplexing and automated calibration for quality assurance. The whole system, consisting of an IONICON PTR-MS and the purpose-built coupling system, proved to be very robust. It has been up and running at different industrial test sites for several years. This setup has now been incorporated in IONICON's PTR-MS bio system, offering an integrated PTR-MS solution, optimized for the biotech industry.

PROCESS CONTROL AND OPTIMIZATION

Knowledge about the underlying microbial metabolism allows to relate monitored signals directly to metabolic activity. This has been demonstrated by Luchner et al. The variation in specific signals can be used to detect a metabolic overload of cells (see figure 3). This opens promising perspectives in terms of advanced process control.

IONICON PTR-MS IN GMP PRODUCTION

After successful testing in research fermentations, the IONICON Proton Transfer Reaction - Mass Spectrometry technology could recently make another important step and has been utilized for real-time process monitoring in an industrial, GMP (Good Manufacturing Practice) controlled fermentation process. The ability to monitor volatile microbial metabolites in the off-gas, without an adaptation to the existing process, has enabled the introduction of PTR-MS to this highly regulated area.

■ Learn more here:
<http://www.ionicon.com/biotech>

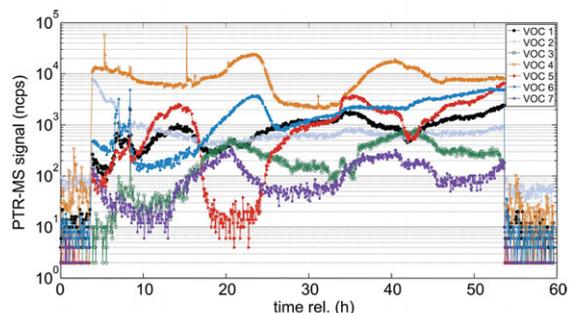


Fig. 1: Typical signals for bioprocess monitoring with PTR-MS. Seven out of 70 volatile metabolites (VOCs) exemplify the distinct variations observed over the course of a fermentation (from Singer et al. Am. Lab. 2011).

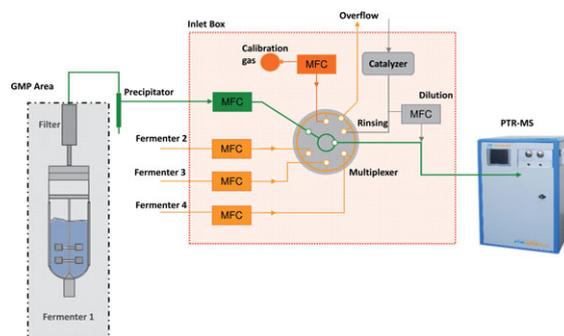


Fig. 2: PTR-MS setup for bioprocess monitoring, including multiplexing, dilution and calibration; now integrated into IONICON's PTR-MS bio system (from Luchner et al., EBR 2014).

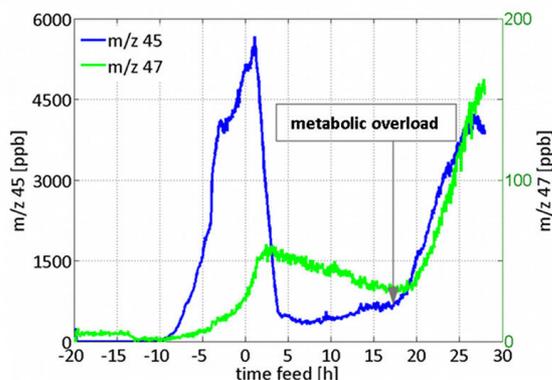


Fig. 3: Signal for acetaldehyde (m/z 45) and ethanol (m/z 47) from a recombinant E. coli fed-batch cultivation, giving information on metabolic overload (from Luchner et al., Biotechnol Bioeng. 2012).