Advanced bioprocess control

Nicro provides turnkey solutions for fermenters

In-line monitoring of metabolites during fermentation processes with Raman spectroscopy

A complete solution—comprised of fermentation system hardware, Raman technology, and analytic services—eliminated time-consuming off-line sampling in favor of real-time monitoring of critical parameters in fermentation processes.

The results:

- Faster process cycle times with less risk due to in-line, real-time process monitoring of metabolites
- Improved process control leading to optimised production and increased yield
- A complete technology packaged solution for fermentation processes

The customer challenges A typical indicator of fermentation progress is the lack of dissolved oxygen in the media which gives an estimation of the process duration. Optical density and metabolites may also be monitored for better insight into the process. Concentration of metabolites would usually be measured off-line with time consuming chromatographic techniques. This off-line sampling approach can bring a potential risk of contamination and lead to the loss of a valuable batch.

Our solutions Nicro combined their competencies together with BIOCentre and Endress+Hauser to provide a complete packaged solution for fermentation processes. It includes:

- Engineering and design of a complete fermentation system from Nicro
- An Endress+Hauser Raman Rxn analyzer and Rxn-45 probe, powered by Kaiser Raman technology
- Analytical services from BIOCentre supported by S-PACT modelling services

nicro

BIOCentre

Nicro[1] is a Croatian company whose tailored bioreactors propelled the rise of pharma, biotech, food and chemical industries in the region. Croatia-based biotech incubator BIOCentre offers infrastructure and consulting for process development, thus enabling commercialization of new products.

"While on-line monitoring the bioprocess, I could pinpoint a time when bacteria switched from one carbon source to the other – the optimal time point to introduce feed and ultimately increase yield. Metabolic switch does not occur always at the same time and on-line monitoring is the only way to know when exactly to intervene."

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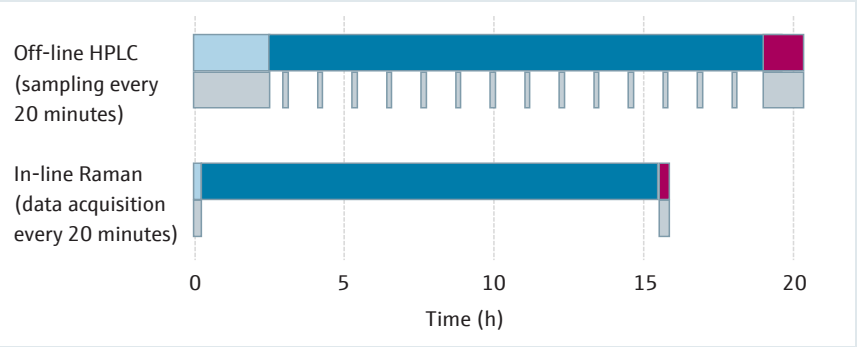
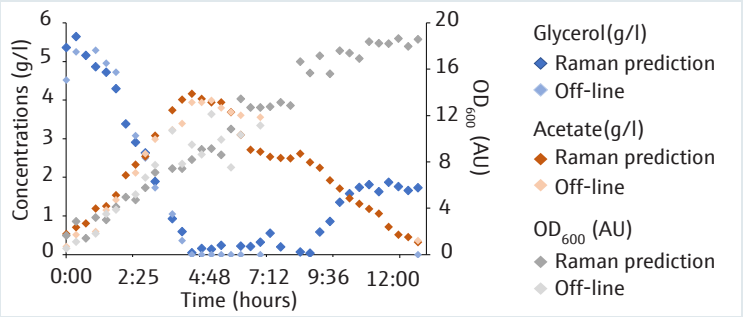
Endress+Hauser

People for Process Automation



In addition to the real-time, multi-attribute measurement of in-line Raman, the faster turnaround time of a Raman-monitored fermentation would increase plant productivity by 33% over a 10-day period.

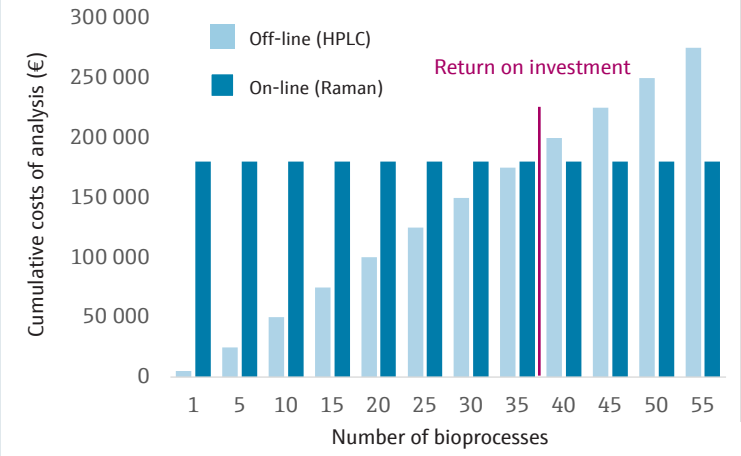


In-line and off-line measurements of acetate concentration, glycerol concentration, and OD600 during a fermentation process.

Optimised process control Direct in-line monitoring of glycerol concentration as input metabolite, acetate concentration as byproduct, and biomass growth provides a better understanding of the fermentation process. The complete fermentation package enables real-time and optimal control of the process, leading to reduced time between batches, limited risk of contamination, and increased yield.

Return on investment after 35 fermentation processes The implementation of in-line analytical monitoring solutions has a significant impact on operating costs, productivity, and safety. Raman systems can monitor several parameters simultaneously with one single probe installed directly in-line.

Calculation of costs based on the purchase and use of a single channel Raman Rxn analyzer at 785 nm and Rxn-45 probe for monitoring glycerol and acetate concentrations, and OD600 for biomass growth compared to the costs of testing off-line samples.



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