

Nicro 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.”

Adriana Lepur, PhD  
Head of Microbiology Laboratory  
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## Advanced bioprocess control

### Nicro provides turnkey solutions for fermenters



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

**From time consuming sample analysis to real-time monitoring of critical parameters in fermentation processes thanks to complete solutions from hardware to development and analytical services.**

#### The results:

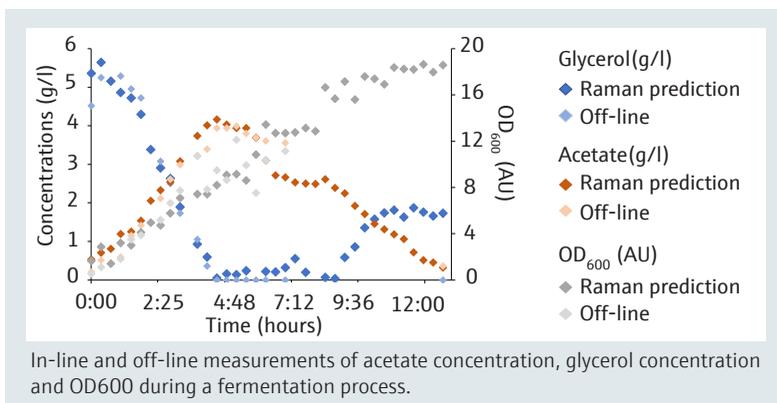
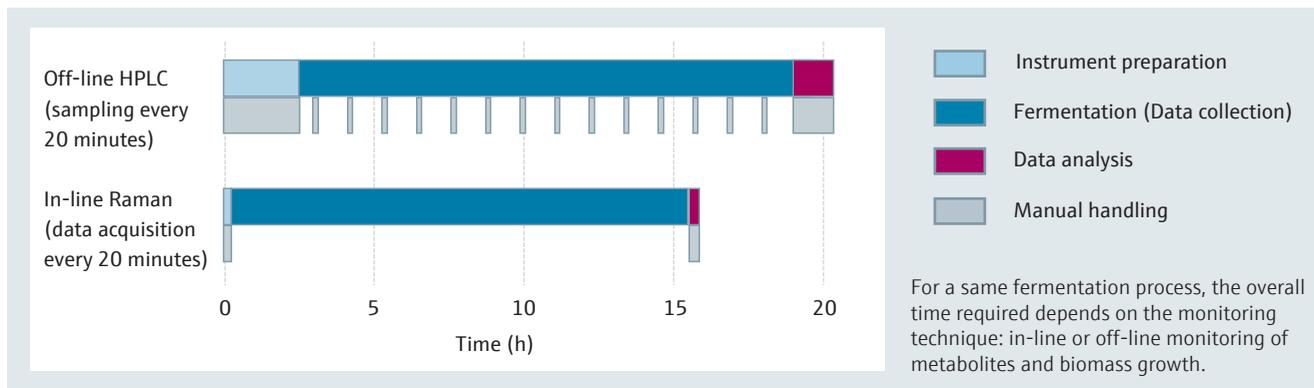
- Safe operation and time saving thanks to in-line process monitoring of metabolites without the need for sampling
- Improved process control leading to optimised production and increased yield
- Complete packaged solution for fermentation

**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 a better insight into the process. Concentration of metabolites

would usually be measured off-line with time consuming chromatographic techniques and therefore would require samples. This can also 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:

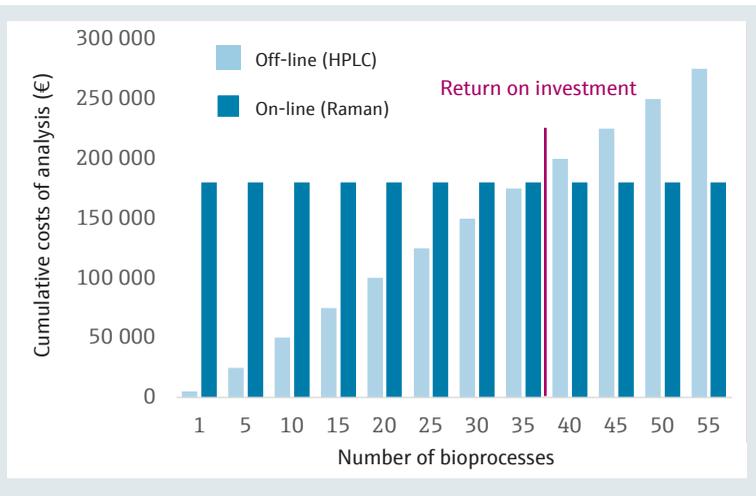
- Engineering and design of complete fermentation system from Nicro
- Kaiser Raman Rxn™ analyzer and BioProbe from Endress+Hauser
- Analytical Services from BIOCentre supported by S-PACT modelling services



**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. Kaiser Raman solutions 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 Kaiser Raman Rxn systems at 785 nm and Kaiser Raman BioProbe for monitoring glycerol and acetate concentrations, and OD600 for biomass growth compared to the costs of testing off-line samples.



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