

High-Throughput Sample Processing and Analytics of Samples Derived from High-Throughput Down Scale Bioreactor Systems



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1 – Background

USP challenges:

High level process understanding and multivariate statistical approaches require elevated data density & a high number of experiments.

High-throughput (HT) cultivation systems, e.g. ambr15/ambr250 (Sartorius Stedim Biotech) are implemented.

Bottleneck:

Large amounts of samples & data are generated.

Need for fast HT sample processing and analytics.

2 – Benefits of HT cultivation systems

- Automation & parallelization of cultivations
- Single-use equipment, short set-up time
- Fully pH and DO controlled systems
- Automated collection of process samples
- Increase of fermentations that can be handled by one employee in parallel

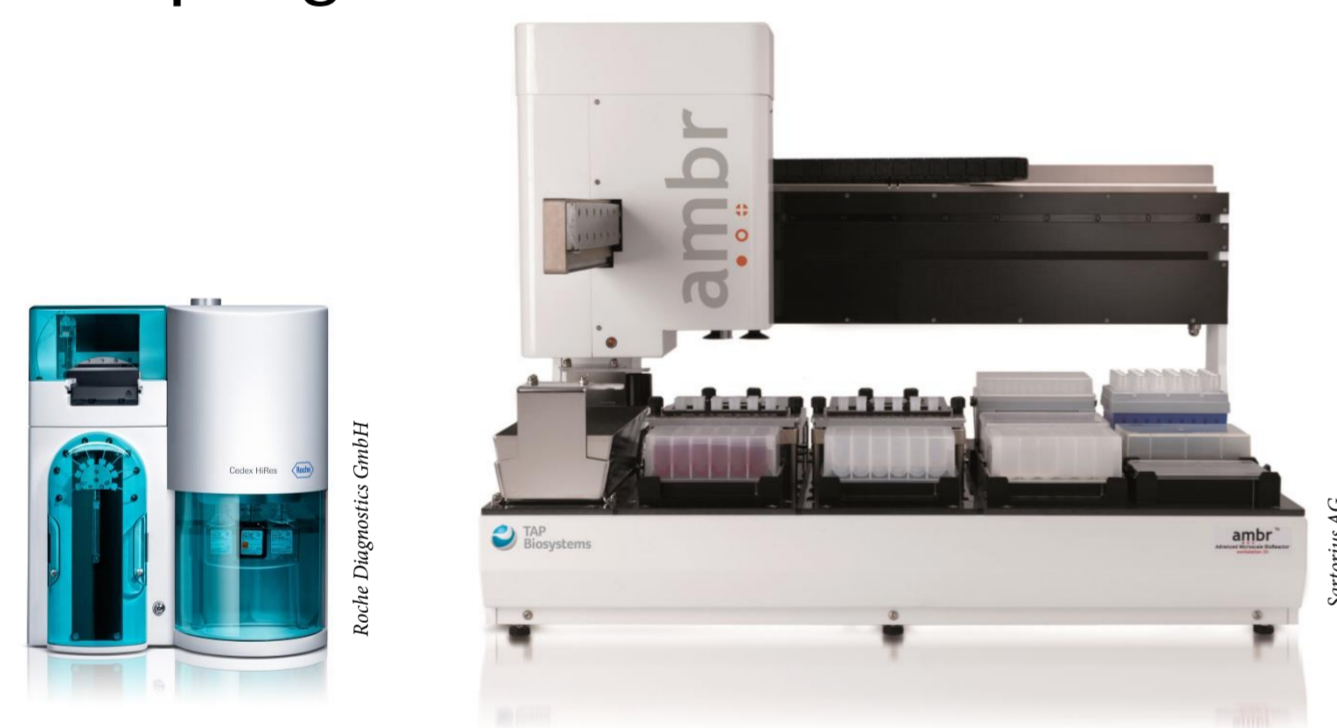


3 – Bottlenecks caused by HT cultivation systems

- Strong increase in number of generated samples
 - About 400 samples have to be handled by one person in a 14 d cultivation
- Strong increase in generated amount of data
 - About 0.7 million data points/48 vessels for a 14 day cultivation for online pH and DO readings
 - Over 5000 data points generated by offline analytics

4 – Tecan Fluent780 links ambr systems & Cedex Bio HT Analyzer

Automated cell counting, pH measurement and sampling to 96 well plates



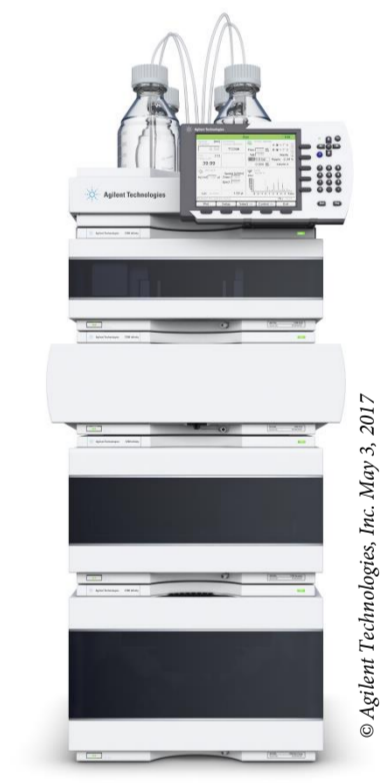
Tecan Fluent780

Automated centrifugation, dilution and distribution of supernatant to different analysis cups



Automated sample preparation & dilution for amino acid analysis & product quality assays

Agilent Technologies RRLC 1290: Amino acid analysis

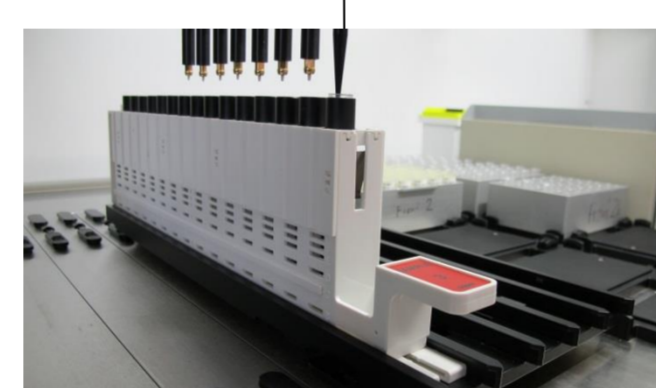


Tecan Evo: Protein A μ -purification, sample preparation for CE-SDS, SEC



Sample volume 50 μ l

Gonotec Osmomat: Osmolality



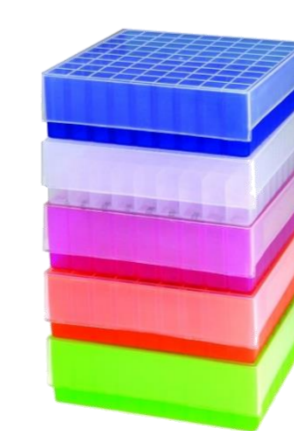
Sample volume 150 μ l (1:2 dilution)

Roche Diagnostics Cedex Bio HT Analyzer: Metabolites & Product Titer



Sample volume 100 μ l – 2 ml

Samples for extended analytics



6 – Conclusion

- Tecan Fluent is perfectly suitable to link an ambr cultivation system to a Cedex Bio HT Analyzer
- A fast and automated workflow for accurate and efficient sample processing for 12 – 192 samples is now available
- 48 samples can be processed within 20 minutes (manual processing: 60 minutes); the operator only has to spend about 5 minutes hands-on
- Higher and operator independent accuracy for sample pre-dilution

6 – Outlook

- Connect ambr15/ambr250, Tecan Fluent780, and Cedex Bio HT Analyzer via microplate shuttles or robotic arms
- Establish feedback loop from Cedex Bio HT Analyzer to ambr15/ambr250 via Sm@rtline Data Cockpit (SDC) middleware (AGU GmbH) for automated feeding
- Enable a fast and easy to use data management & analysis system for HT cultivation systems