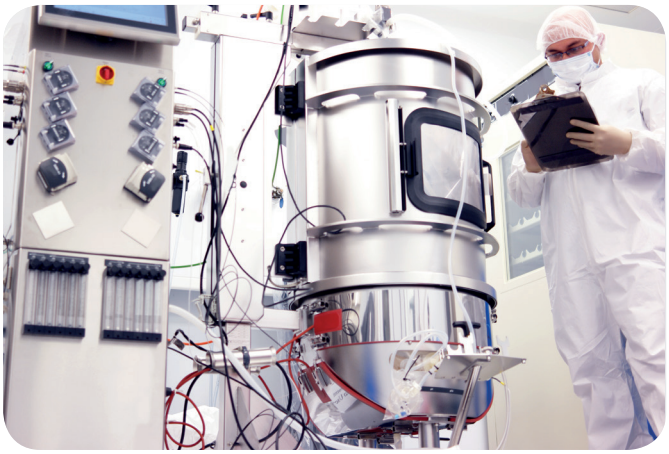


Application Note AN N524

Online Monitoring of Fermentation Processes in Pharmaceutical Industry using FT-NIR Spectroscopy

In the pharmaceutical environment, due to the strict regulatory requirements, the continuous control of fermentation processes is an essential part of the manufacturing process. For years Bruker has been successfully addressing the problem of challenging measuring conditions in fermentation processes by smart technical solutions.

Basis for the synthesis of an active pharmaceutical ingredient (API) are GMOs (genetically modified organisms). Under optimal conditions, they are cultivated in a nutrient solution to maximize cell growth and thus productivity of the organisms. For an optimal result, it is necessary to measure, control and if possible adjust several variables, like glucose, lactate, protein and more during the fermentation process from the start-up media to the final product.

Measurement accessories and software

Fermentations are initially transparent but become increasingly opaque as the cultivation progresses. Therefore, transmission measurements are unsuitable for monitoring the entire cultivation process.

To provide reproducible measurements even for slurries and emulsions, Bruker developed a transflection probe, which combines the benefits of transmission and reflection measurements. In combination with the advanced measuring modes of the MATRIX-F FT-NIR spectrometer, even the presence of gas bubbles will not influence the results. On request, the probe can be adapted to different process conditions. In addition to various flanges, the immersion depth and steel type can be selected accordingly. Also, FDA-compliant sealings as well as fully autoclavable versions are available.

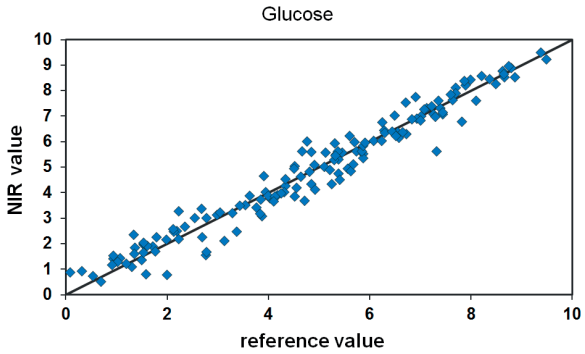
In order to provide ideal solutions not only in the field of electronics and measurement technology, Bruker also offers validated and certified software according to FDA 21 CFR Part 11 for communication with an existing process control system.

Summary

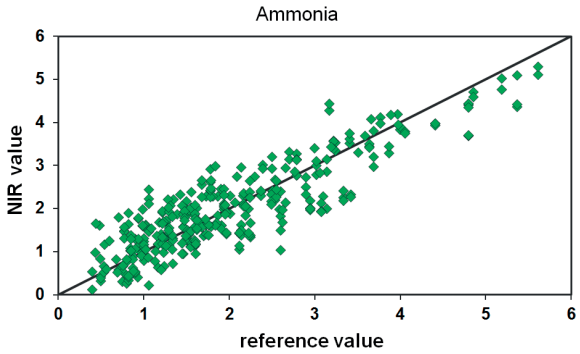
Based on the online measurements of variables such as glucose or ammonia a fed-batch fermentation can be tightly controlled to optimize the results of the process to its maximum.

Parameters commonly analyzed with FT-NIR

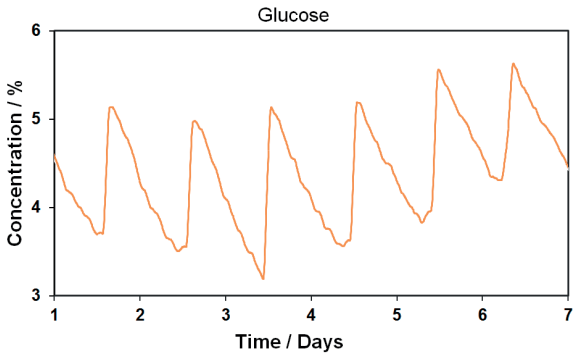
- Glucose
- Ammonia
- Protein
- Lactate
- Carbohydrates
- Cell Number or Density
- Recombinant Protein



Cross validation results of a PLS based model for the online prediction of glucose during a fermentation reaction.



Cross validation results of a PLS based model for the online prediction of ammonia during a fermentation reaction.



Prediction of glucose concentration during a typical fed-batch cultivation.

FT-NIR Spectrometers: Bruker Optics offers various FT-NIR spectrometer models for lab, at-line and on-line applications:

TANGO

FT-NIR analyzer for routine use in the lab.

MPA II

Multi Purpose Analyzer for maximum flexibility.

MATRIX-I

At-line analysis with optional NEMA4/IP66 protection.

MATRIX-F

Process monitoring with probes and sensor heads.

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