Christoph Koeth
Senior Director Innovation, Fresenius Kabi, Austria

Online monitoring of total parenteral nutrition products produced in high-pressure homogenization processes

"With OF2i® we can now go way beyond our previous capabilities and see great potential to replace several devices. We are investing in a future which will provide us with real-time information about the product quality and may deliver insights beyond currently established controls."

Continuous online monitoring of high-pressure homogenization processes

Online monitoring of the particle size distribution (PSD) of emulsions for intravenous application of pharmaceuticals, parenteral nutrition during homogenization to ensure formulation stability.

Challenge

The particle size distribution of parenteral emulsions is a critical quality attribute (CQA).
Christoph Koeth and his colleagues tested a number of sensor systems for online monitoring of their emulsions. A chance meeting with Chris Hill and Gerhard Prossliner from BRAVE Analytics led to the joint collaboration and development of the BRAVE B-Curious online sensor.

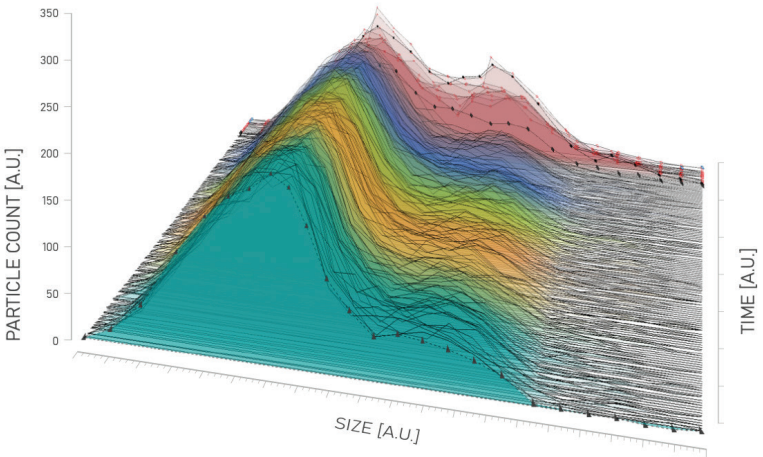
Application highlights

The BRAVE B-Curious online unit (including a continuous and automated online sample preparation unit) was installed in a four-stage homogenization pilot plant. After the first step, the particle size is reduced from 3 µm to approx. 0.3 µm. The process analyzer continuously monitors the PSD distribution and automatically evaluates data such as D-values to assess the efficiency of the first homogenization step.

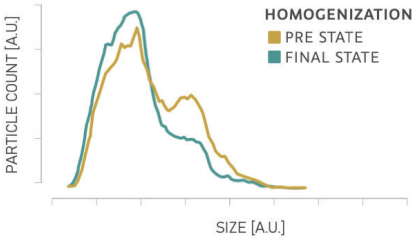
The challenges are:

- The time lag inherent with laboratory measurements leads to inefficient production processes.
- Offline measurements are time-consuming and require qualified personnel.
- Current offline methods provide results too late for process optimization.
- Current measurements do not capture all fluctuations and anomalies.

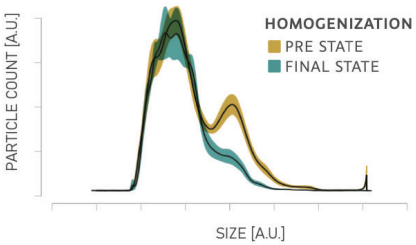
- The values are sent to the LIMS every 20 seconds.
- A better understanding of the homogenization process leads to more efficient production and huge savings in product waste.



▲---▲---▲ Particle size distribution process control for final homogenization state every 20 seconds
♦---♦---♦ Fault detection within homogenization process detectable as immediate shift in particle size distribution



OFFLINE STD. REFERENCE MEASUREMENT
(NANO PARTICLE TRACKING ANALYSIS)



OF2i® time-resolved online characterization as number-based size distributions versus nanoparticle tracking analysis of different processing steps in looped emulsion production. Timestep 10: fault detected within homogenization. © BRAVE Analytics & Marko Šimić