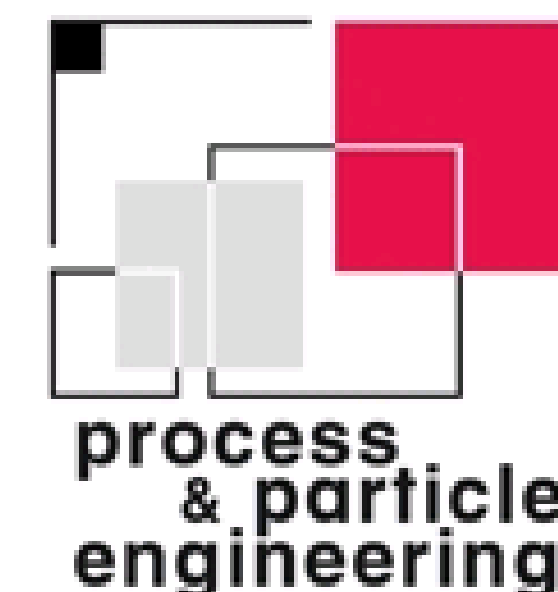


Quantitative Quasi-simultaneous and Spatially Resolved Real-time Monitoring of Powder Mixing Processes with a Multiple NIR-Probe Setup

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Introduction

Spectroscopic techniques, like near-infrared (NIR) spectroscopy, are practical for online monitoring and process control, because of their non-invasive and fast analytical capabilities. To analyze the spectroscopic data, high performance algorithms and advanced methods of modeling are required. Here, we present results on quantitative in-line and real-time monitoring of powder mixing processes by near-infrared (NIR) spectroscopy [1]. Spectral data were collected with an FT-NIR Spectrometer and data analysis was performed with Matlab and The Unscrambler (Camo) following different strategies with multiple probe setups for determination of the mixing end-point and for a spatially resolved monitoring of the powder flow kinetics within a blender.

Methods

Multi-Probe NIR Setup

optical fiber multiplexer
statistical data analysis
Content
Process Time
FT-NIR Spectrometer
optical fiber probe

Mixing vessel with measurement ports

Monitored Positions
fill level H
CH6
CH5
CH4
CH1 CH2 CH3
D=100 mm

Dynamic Calibration and Model Building

Design of Experiments (DoE) calibration for pharmaceutical powders Lactose Monohydrate (LM), Acetylic Salicylic Acid (ASA)
Tubular mixer processed calibration samples
Dynamic calibration on rotating table to address sub-sampling issues
Simultaneous and standardized dynamic calibration for 6 fibers

Optical fiber reflectance probe with sealed sapphire window

Flexible process monitoring at positions critical to quality

Fiber switch box for multi probe handling

Experiments

Characterization of the Multi-fiber System

To find the spectral integration time of best performance for 4 RPM impeller speed, a series of measurements was performed. The results of the mathematical analysis shown on the right give the summation of the overall spectral variance versus the number of integrated spectra of 0.3 s each. As a result, the integration time was set to 12 spectra, i.e., 4 seconds.

All spectral data were screened and pretreated with a Matlab algorithm to align spectral resolution and file formats for further processing with The Unscrambler (Camo). Data preprocessing involved spectral averaging and reduction to a spectral band ranging from 7200 cm⁻¹ to 4500 cm⁻¹ and Standard Normal Variate (SNV) normalization. A quantitative model was developed applying Partial Least Squares Regression (PLS) with cross validation.

	Slope	Offset	RMSE	R-Square
channel 1	0.978281	1.115035	3.768134	0.978281
channel 2	0.955791	3.063074	4.003345	0.971320

In-line Monitoring of Powder Mixing Endpoints with NIR Spectroscopy

Models Performance

The given values for the models show the mathematical quality of the model, but not the real predictive performance. To evaluate an existing model we measured calibration-grade (Turbula mixed) samples and compared the predictions with the mixture values. The highest influence seems to result from different fiber positions between calibrations.

Two sets of six models (one for each channel) were developed from different datasets. A mixing experiment with 80 g ASA on 20 g LM was performed and monitored by the NIR system in-line at six different positions. The results were predicted on the basis of the two different model sets.

The predictions of the data with two model sets show the same approximation behaviour of the mixing end point but different offsets. However, the process monitoring with multiple NIR probes at different positions allow simultaneous investigation of the overall mixing dynamics.

Conclusions

- Simultaneous and standardized dynamic calibration for 6 fibers were performed.
- Spatially resolved in-line measurements at critical positions enable monitoring of the mixing behaviour, although predictive models show different offsets for the mixing end-point.
- For this reason, the validation of models has to be improved and further development is needed.
- Process monitoring with multiple NIR Probes at different positions allows as demonstrated simultaneous investigation of the overall mixing dynamics.