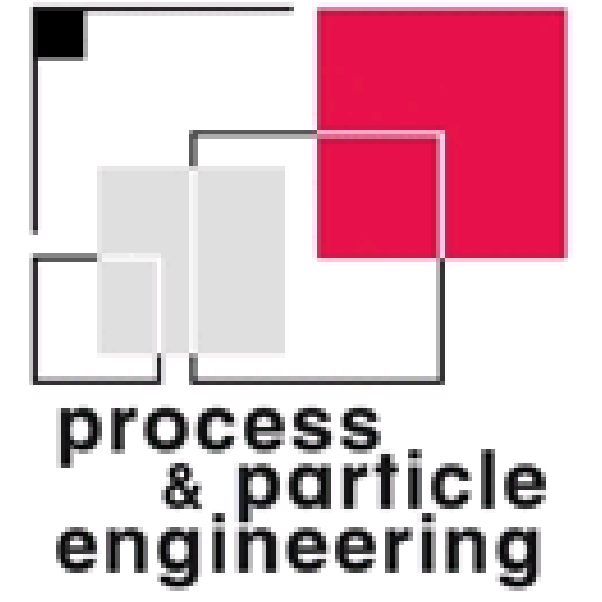


# NIR Spectral Imaging for the Pharmaceutical Industry

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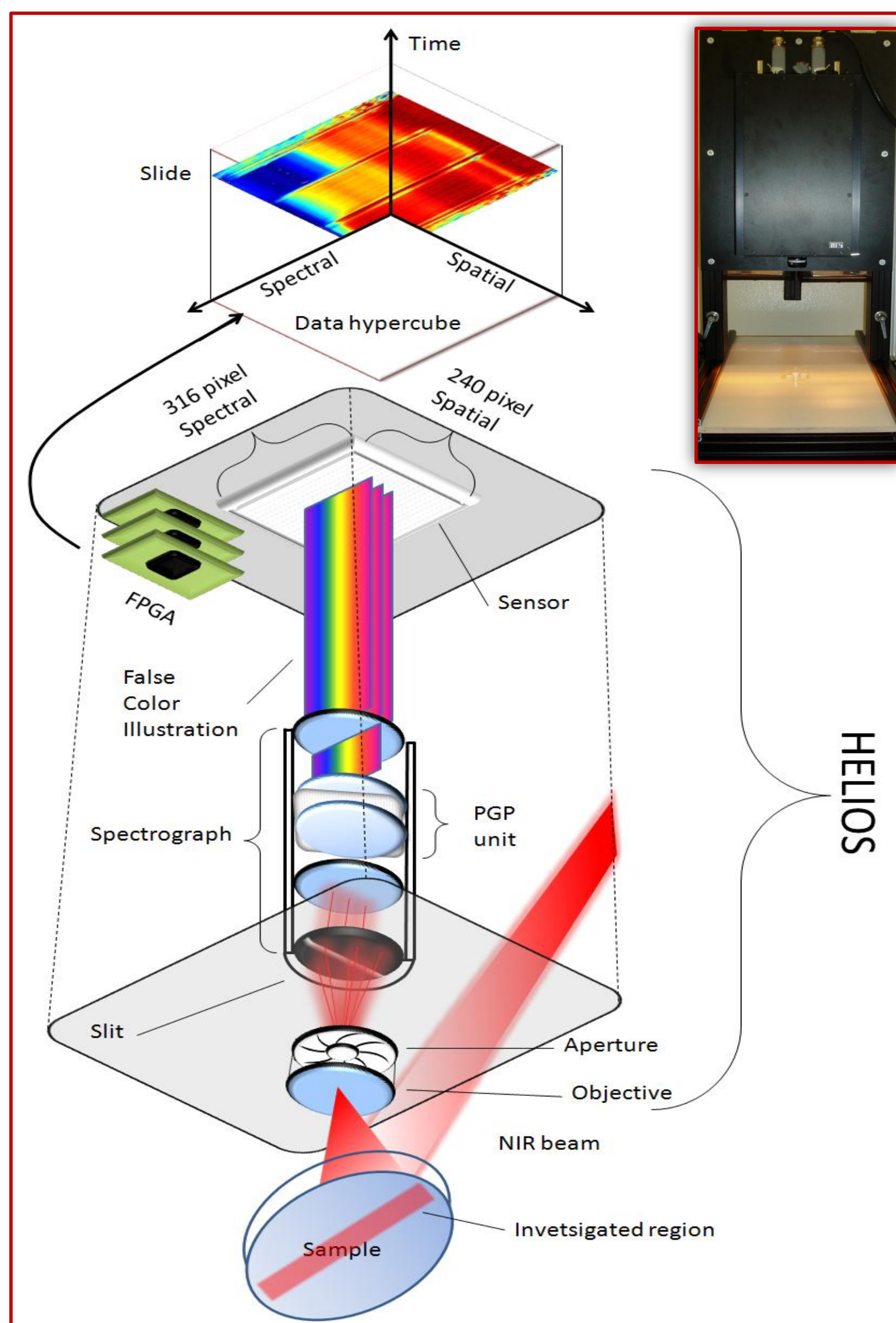
## Introduction

In order to fulfill the quality requirements introduced by regulatory authorities for pharmaceutical products, reliable methods are needed for the product qualification. Many process analytical technology (PAT) tools satisfy the requirements, such as non-destructive and sensitive determination of material properties. Especially continuous manufacturing processes (e.g., mixing, extruding, etc.) show demand on fast process monitoring systems with the capability for real-time and in-line measurements.

Here, a near-infrared (NIR) spectral imaging system (Helios Core from EVK DI KERSCHHAGGL) with an InGaAs detector (240 spatial x 316 spectral pixel) was tested for its applicability in the pharmaceutical industry. The system characterization was performed in order to examine detection limits for low active pharmaceutical ingredient (API) content in powder blends, moisture content or the coating thickness of tablets. Multivariate data analysis (MVDA) was applied for qualitative and quantitative characterization.

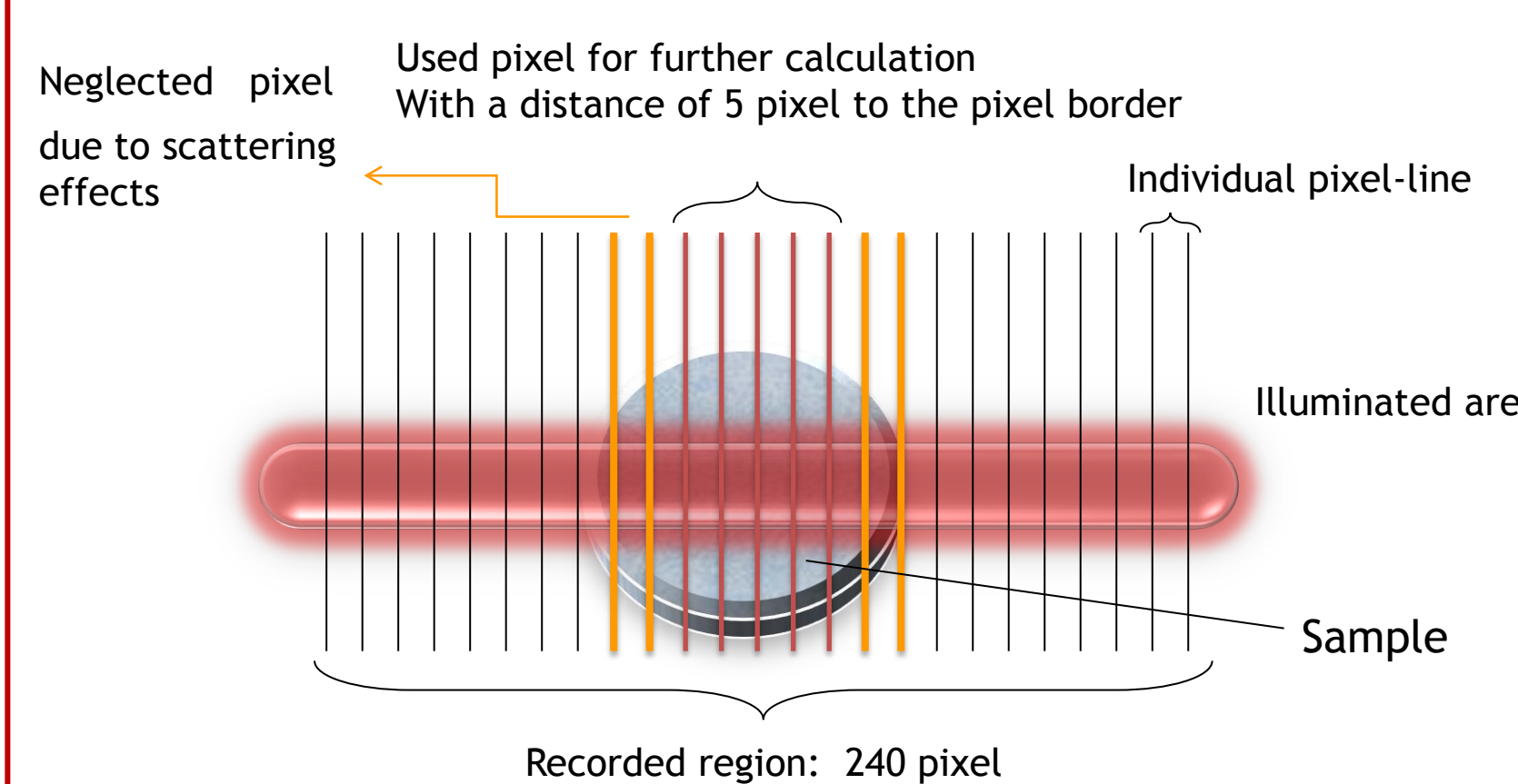
## Methods

### NIR Camera HELIOS



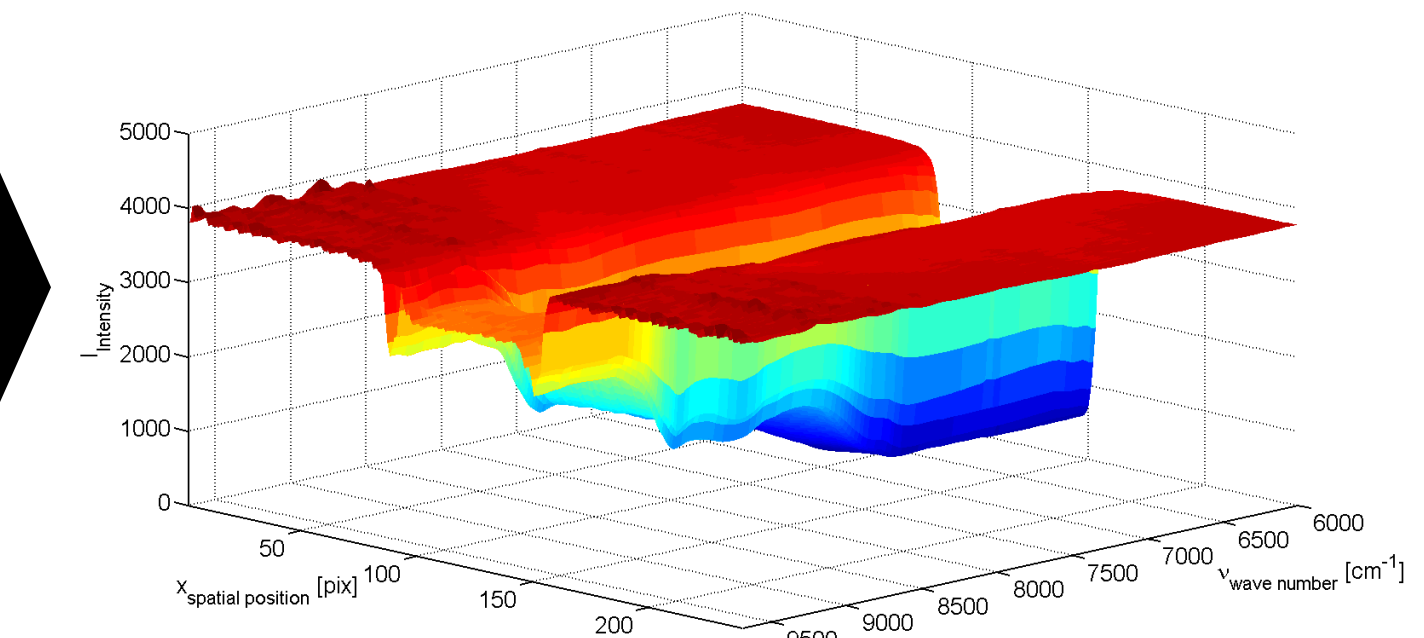
- NIR Chemical Imaging HELIOS from EVK GmbH.
- Sampling rates up to 333 pictures per second enable monitoring of fast processes.
- Spectral pretreatments with integrated FPGA or multi variate data analysis software.
- System was evaluated for the applicability as a PAT-tool for pharmaceutical products, e.g., powders, liquids, tablets, etc.

### Chemical Imaging and Pretreatments



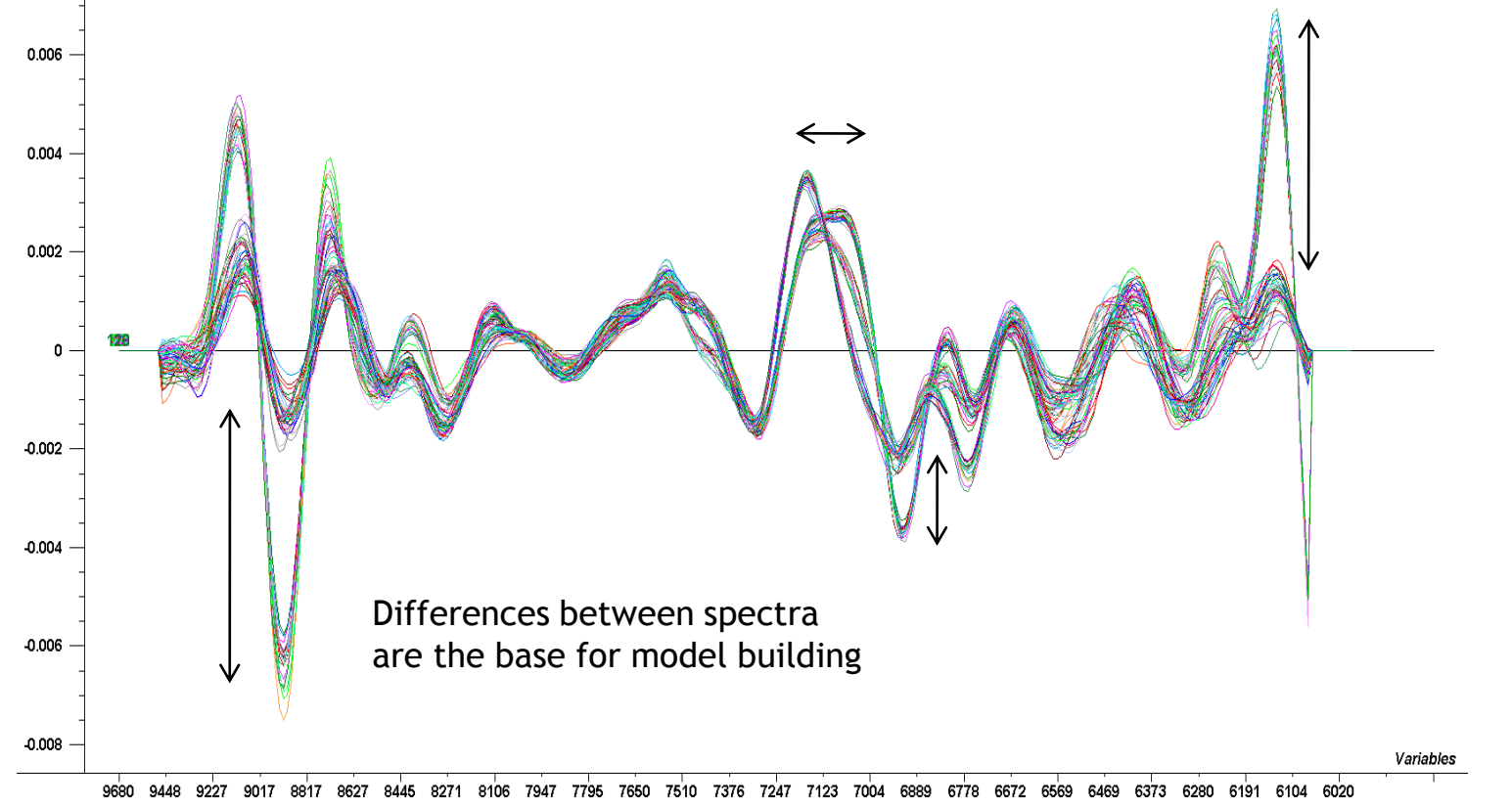
- After the selection of the appropriate region of interest (ROI) in spatial and spectral direction further processing can be performed
- Integrated pretreatment routines for the correction of an inhomogeneously illuminated sample area.

### 3D Representation of the Chemical Image



- Different preprocessing effects allowed accurate modeling.
- The application of Standard normal variate (SNV) and second derivation leads to better distinction between spectra.

### Second derivate



## Experiments

### Powder Blends

- Visually indistinguishable powders can be identified quantitatively
- Wrong referencing may lead to model inconsistency and a low model performance.

One reference for an area of individual spatial pixel-lines

$\Sigma=100\%$  ASA  $\Sigma=100\%$  MCC

Model improvement	Slope	Offset	RMSE	R <sup>2</sup>	Reduction Factor
Calibration	0.96	1.30	5.58	0.96	1
Validation	0.96	1.32	5.71	0.96	1
Calibration	0.97	1.11	5.15	0.97	2
Validation	0.97	1.13	5.38	0.97	2
Calibration	0.97	0.94	4.75	0.97	4
Validation	0.97	0.97	5.13	0.97	4
Calibration	0.98	0.85	4.50	0.98	10
Validation	0.98	0.78	5.07	0.97	10

■ By averaging the spatial pixel-lines the model can be improved.

### Moisture Content of Tablets

- Tablet moisture is a quality control parameter in manufacturing that was used for referencing the PLS1-models. The physical parameter used for calibration was the weight of loss.

	Slope	Offset	RMSE	RMSE [%]	R <sup>2</sup>
Calibration	0.99	0.01	0.05	4.3	0.99
Validation	0.98	0.01	0.05	4.6	0.99

- Up to 3 PCs were used for the evaluation of the model performance.
- The model performance for the predictability of the parameter moisture content was calibrated by the loss of weight.

### Tablet Coating Thickness

- The endpoint for a tablet coating process may be confirmed by in-line near infrared monitoring.
- Here, differently coated tablets were taken from the coating process and the coating thickness was determined at the micrometer scale.
- A baseline correction, standard normal variate and second derivate were applied in order to improve the model stability and performance.
- With an appropriate selection of preprocessings, as demonstrated here with a linear baseline correction, the effect of monitoring position can be corrected.

	Slope	Offset	RMSE [mm]	RMSE [%]	R <sup>2</sup>
Calibration	0.96	0.001	0.0044	7.42	0.96
Validation	0.96	0.001	0.0047	7.90	0.96