SpecAnalyzer
Tool for monitoring solid state transformation

Introduction

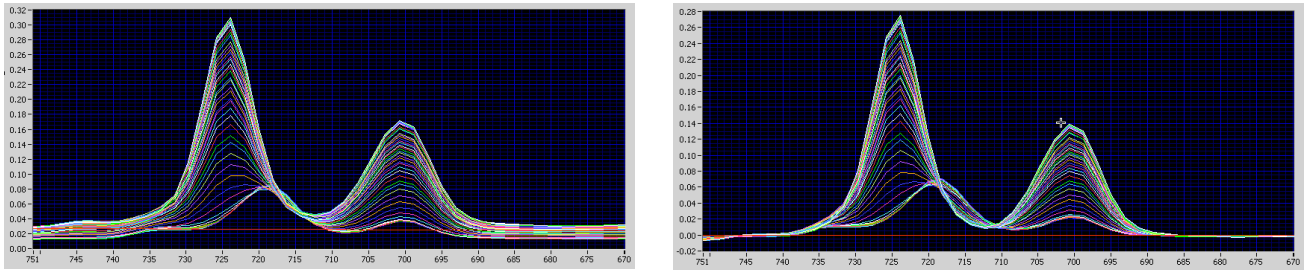
During the last decade spectroscopic-based techniques for on-line monitoring of chemical processes has become a powerful tool to support process development, quality control and process safety in production. However, these process analytical techniques (PAT) often require cumbersome and time-consuming elaboration of spectroscopic calibration models which then frequently must be (re)validated as even small changes, e.g. caused by solvent recycling, can have significant effects on the results obtained. Systematic integration of the process know-how of process chemists/engineers into the calibration model can contribute towards generating advanced calibration models with improved reliability and robustness. Following this approach, RPD TOOL's SpecAnalyzer makes it possible to combine chemical process know-how with statistical analysis of spectroscopic data sets and to elaborate robust and reliable calibration models in a fast and straightforward way.

Interactive analysis of spectroscopic data

SpecAnalyzer consists of a set of graphical user interfaces to perform step-by-step analysis of small and large spectroscopic data sets. The sophisticated set-up of the program supports the user in the generation of calibration spectra sets, the choice of data pre-treatment (e.g. baseline correction, spectra normalisation, etc.) and finally the elaboration of robust and reliable calibration models in an interactive and intuitive way. This enables fast and straightforward development of robust and reliable spectroscopic models which most often are superior to models generated by black box methods without the possibility of integrating process know-how. The following example gives a brief insight into the software and demonstrates how easy spectroscopic modelling can be.

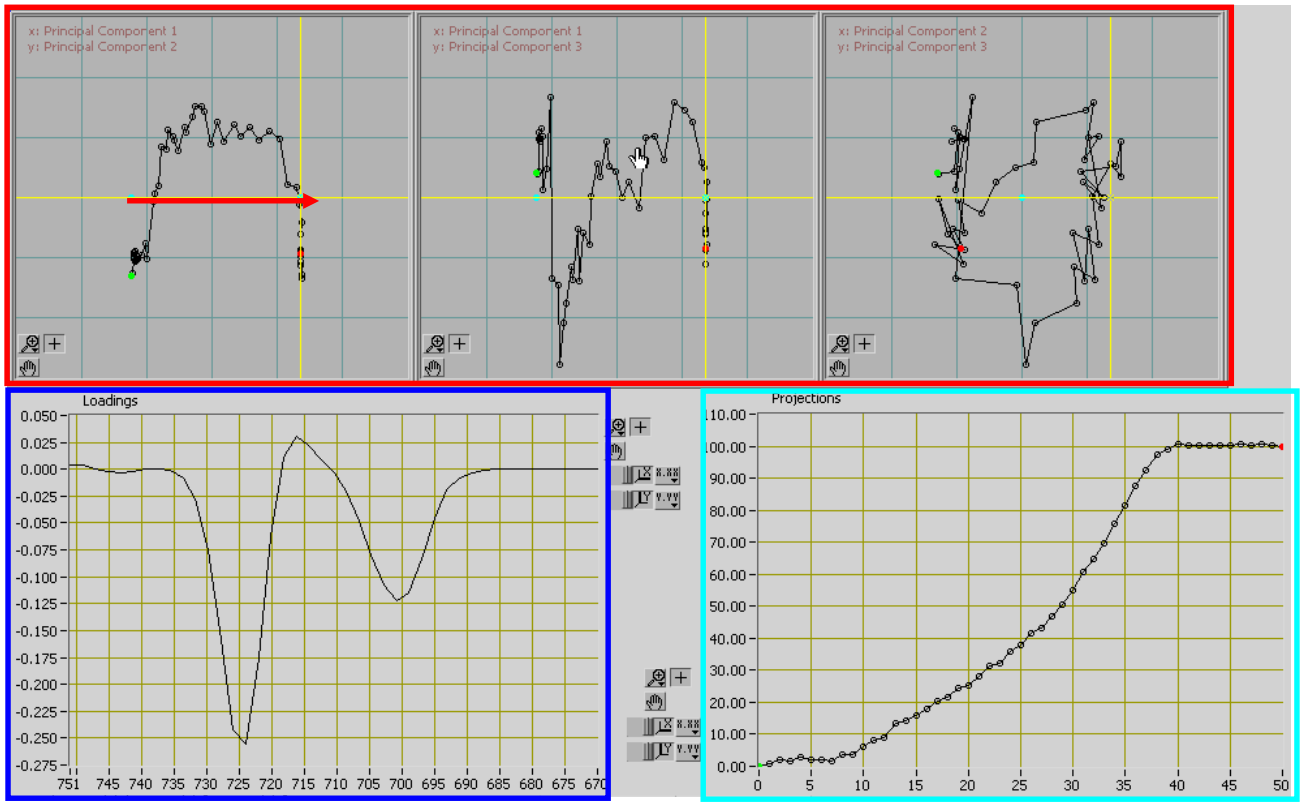
Monitoring the slurry transformation of a solid state

The first steps of the analysis of a spectroscopic data set from a slurry transformation of a solid state of a drug consist in the selection of the spectroscopic data set and the choice of spectra pre-treatment such as baseline correction or spectra normalisation (plot 1).



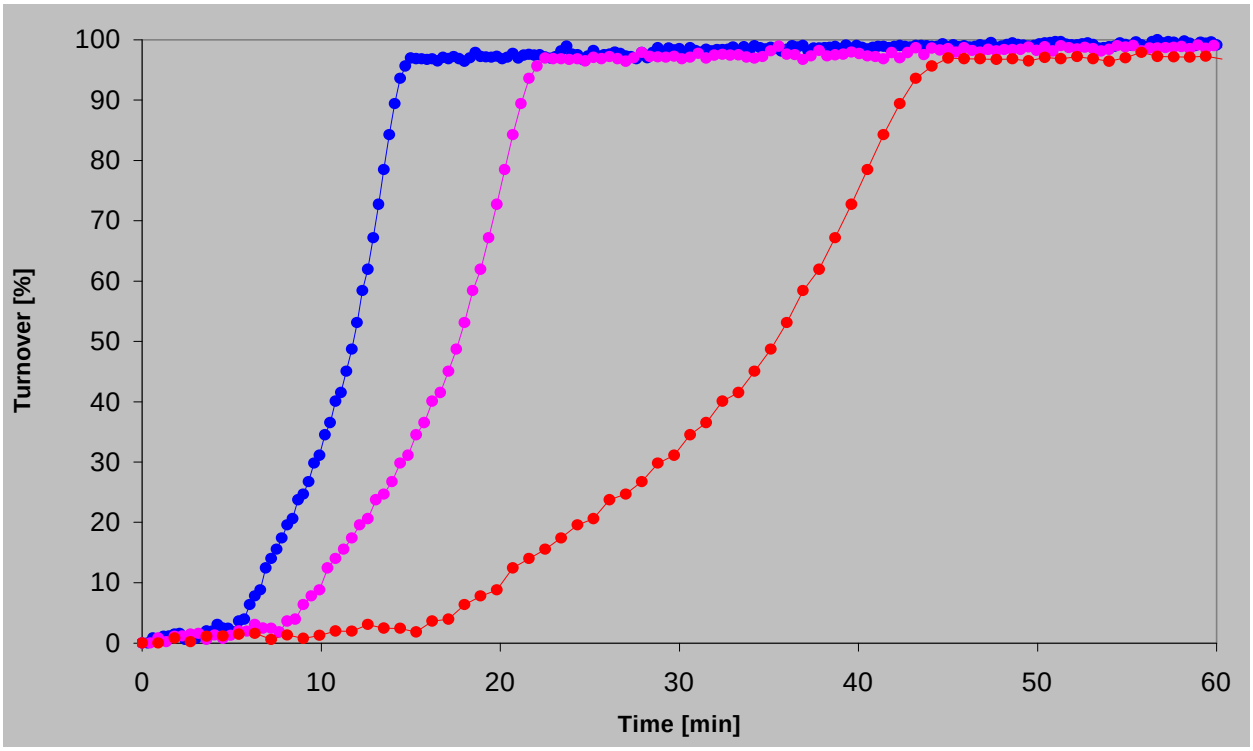
Plot 1: Spectra pre-treatment: left raw spectra, right baseline corrected spectra. X-axis: wave number [cm-1].

After the selection of the wavelength ranges, the spectra analysis continues with principal component analysis. The result of the principal component analysis is shown in plot 2. A scatter plot of the first 3 principal components (red frame in plot 2) spans the spectra space where a spectroscopic model with up to three calibration points can be interactively defined. In this example, a two-point model along the 1st principal component is chosen (red arrow in plot 2). The loadings show the selected model in the spectra space (dark blue frame). In addition, the projections represent the corresponding kinetic profile (light blue frame).



Plot 2: Result of the principal component analysis. Red frame: scatter plot of the first three principal components. Each point represents a spectrum and all spectra are lined in chronological order (first spectrum green, last spectrum red). Dark blue frame: spectroscopic model. Light blue frame: kinetic profile (projections)

Rational verification of the loadings and projections is required to ensure the robustness of the spectroscopic model. The loading generally reflect spectroscopic differences between the initial and the final state of the process which must in this case correspond with the differences in the Raman spectra of the two polymorphs. In addition, the kinetic profile shown in the projection is typical for re-crystallisation processes where the precipitation of the new solid state starts slowly after temporary super-saturation of the solution of the new polymorph and then continues with increasing speed. The elaborated model is now ready to monitor the slurry transformation of the solid state of this drug compound. Plot 3 shows the result of different transformations performed during process optimisation in lab-scale experiments:



Plot 3: Kinetic profile of different batches with slow (red), intermediate (pink) and fast (blue) kinetic of the transformation process.

Benefit

The combination of practical process know-how with statistical analysis provides spectroscopic calibration models for process monitoring in a fast and straightforward way. The interactive windows of the software enable a scientific rationalisation of the elaborated model and ensure the robustness and reliability of the models without the need for time-consuming reference analytics of a large number of test samples.

Please do not hesitate to contact us for further details of our unique software tools for chemical and physical process monitoring.

Your RPD TOOL Team