Chemometrics

Application Note

Kinetics Study with Raman Spectra

Abstract

A series of Raman spectra were collected to follow the formation of a product and any intermediates that might be present. The dataset contains 200 spectra collected over the course of the batch reaction, each spectrum spans 4,300 wavelengths. The source of the data is confidential as is the application, but it serves as an introduction of the use of chemometrics processing, specifically the application of Alternating Least Squares (ALS) mixture analysis to identify and quantitate the ingredients, intermediates and products of a fast reaction.

The data was supplied in SPC file format, compatible with Pirouette. During data collection, there was a process upset, affecting the spectra, therefore, only the data following the upset were analyzed initially. An overlay of these 129 spectra is shown in Figure 1.

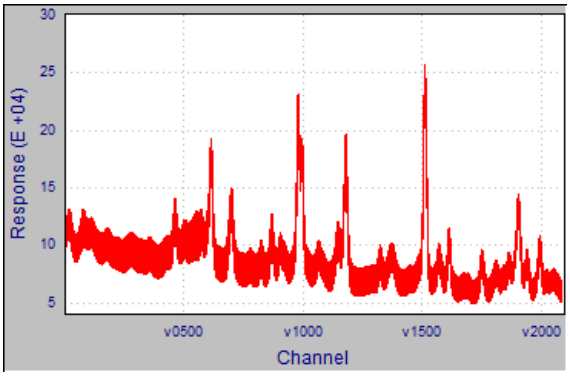

Figure 1. Original Raman spectra

This overview of the data reveals considerable scatter among the spectra. This magnitude of baseline offset could have a significant impact on subsequent processing, therefore, the spectra were first transformed by normalizing (using an area % normalization) so that differences in the samples would be less tied to the scatter and more accessible to interpretation.

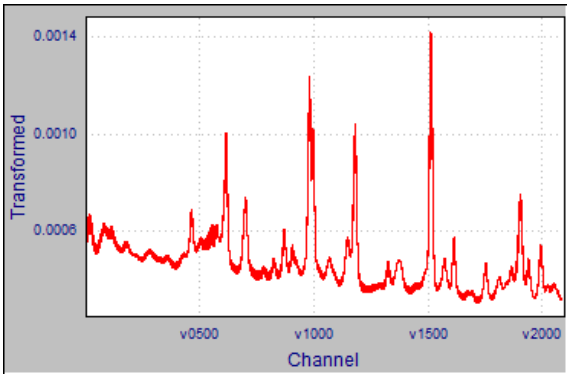

Figure 2. Normalized Raman spectra

A principal components analysis was run on the normalized spectra and the resulting scores show clear trends as the sample reaction proceeds. Between the start and end of the reaction, there are two distinct nodes that implicate the existence of reaction intermediates. The reaction sequence depicted in Figure 3 starts at the top of the plot.

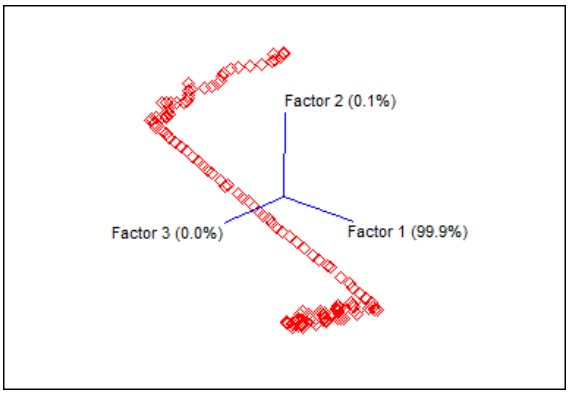

Figure 3. PCA scores of the spectra during the reaction

Running ALS on the same normalized spectra reveals the intensity profiles of four materials as seen in Figure 4.

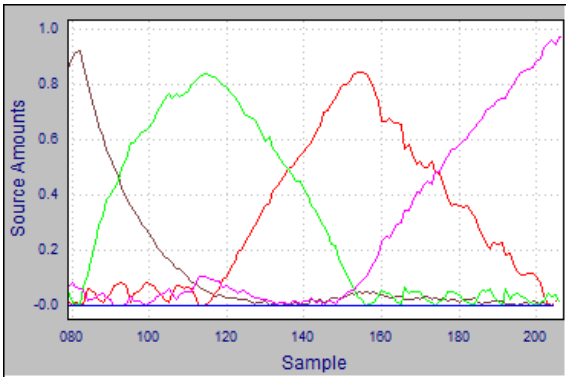

Figure 4. Reaction profiles from ALS

The corresponding spectra of the four source materials are quite similar, with overall structure dominated by the solvent as seen in Figure 5. The starting material is the brown spectrum, intermediates 1 and 2 are green and red and magenta is the final product.

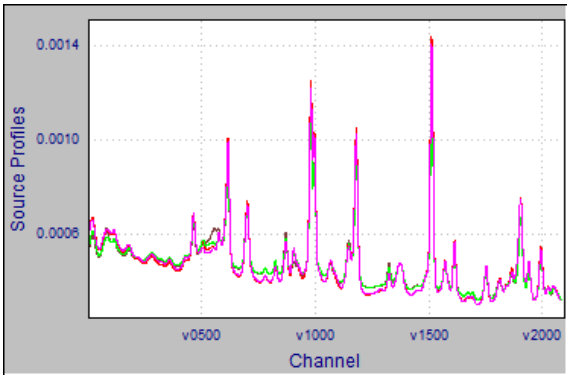

Figure 5. Reaction spectra from ALS

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Zooming in to the beginning spectral region more clearly shows where differences among the spectra can be observed. In particular, the intensities near variable 550 decreases as the reaction proceeds.

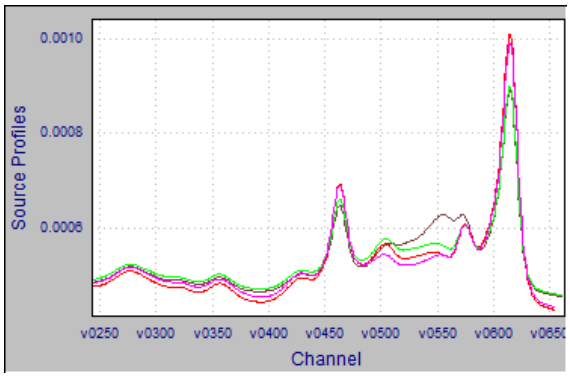

Figure 6. Key Raman shifts during reaction

Note that at any point along the reaction timeline, it is possible to get relative quantitative information on the concentrations of the evolving species. In this way, even very fast reactions can be monitored non-invasively.

After successfully deconvolving the mixture in this reaction, an attempt was made to do the same for all of the data, including the interruption. So, the early data were put back in and another PCA was run. The scores from this analysis show the same group of spectra as in the unperturbed data (the red points) but now include two additional groups of spectra: one set before the reaction begins (brown points) and another after the reaction begins but before the upset occurred (green points).

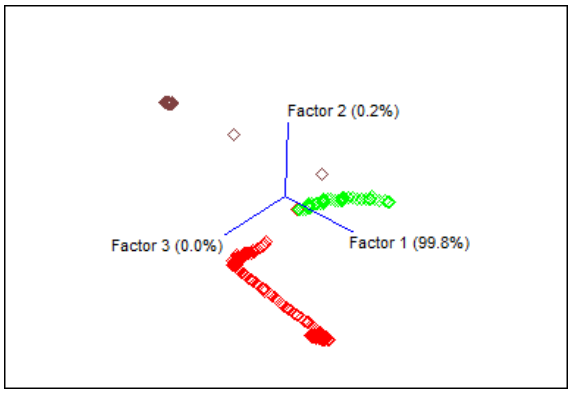

Figure 7. PCA scores from all data

In addition, there are spectra in the transition from the pre-reaction to the reaction start that show as separate individual points.

Results from an ALS on the full data set now show the pre-upset regions as mostly constant concentration bands before the reaction products begin to evolve.

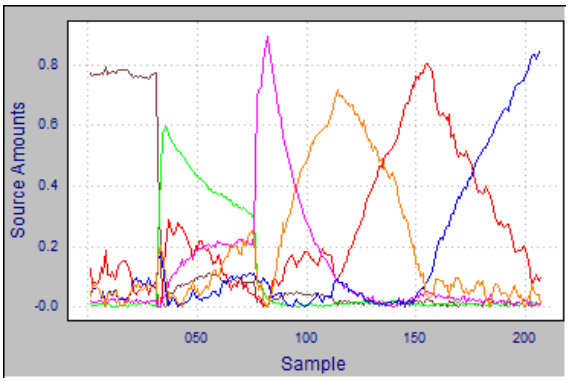

Figure 8. Reaction profiles from before and during the actual reaction

And the spectra proposed by ALS for these pre-reaction regions are clearly different than those during the reaction, as seen in Figure 9, below.

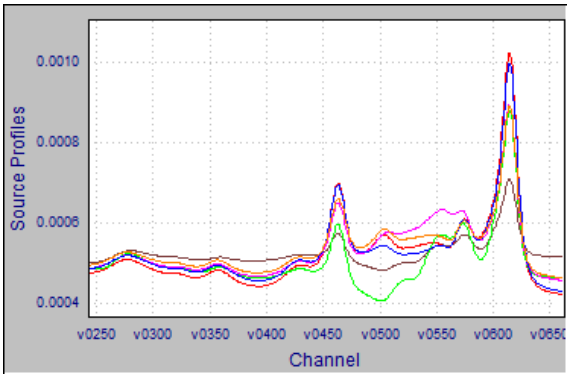

Figure 9. Changes in Raman spectra before and during reaction

Here the brown and green source profiles correspond to the early regions in the reaction progress plot shown in Figure 8. There is no change in the spectral shapes of the 4 reaction products shown earlier, as should be the case.

Thus, the multivariate tools used here can be used not only to monitor reaction progress but also to flag unexpected behavior in a reaction.

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