Success story

OPLS for Efficient Identification of Batch to Batch Process Variation

Orthogonal Partial Least Squares (OPLS), a more recent and less well known modeling method for multivariate regression, has distinct benefits over traditional PLS modeling for some applications. Kaiser Optical Systems, Inc., a leading manufacturer of Raman spectroscopy equipment, embeds SIMCA®-Q software - part of the Umetrics® Suite of Data Analytics Solutions - in its Kaiser RamanRxn Systems™ Analyzers. Sartorius used Kaiser Raman spectra data collected from in-line monitoring of batch cell culture processes to compare the results of regression analysis using OPLS versus PLS modeling.

Enabling Real-Time Process Control

In bioprocessing, one goal is to achieve the highest possible yields of quality product in a cost- and time-efficient manner. This can best be accomplished by having a well-designed, well-defined, and well-controlled process. Key developmental strategies for meeting this goal include the application of Process Analytical Technology (PAT), which includes the use of process modeling tools to identify and analyze batch-to-batch variation and of in-line monitoring of process variables and feedback of results to optimize process parameters.

Raman is a vibrational spectroscopy technique that is ideally suited for bioprocesses because of its specificity and minimal water interference. Kaiser Raman is a reliable and robust PAT for bioprocess development and use in a cGMP setting, shown to increase product titer and impact product quality. It is a platform technology equally suited for cell culture and fermentation. Raman-based bioprocess control may increase product titer and impact product quality. Kaiser Raman is proven to be an important component of the bioprocess workflow for enabling real-time monitoring and control.

Choosing the Right Software Tool for Your Data

"Regression analysis is deployed both for batch evolution and batch level modeling," says Anna Persson, Senior Principal Data Scientist, Sartorius Data Analytics. Multivariate methods to aid in analyzing process data, such as PLS and OPLS, are part of the Sartorius's SIMCA solution. The PLS method of multivariate analysis dates back to the 1970s and was updated in the early 1980s. OPLS is a more recent, modified algorithm, introduced in early 2000s, which sometimes offers enhanced model interpretation.

While both PLS and OPLS are designed to capture batch-to-batch variation, here more efficient separation between batches is achieved with OPLS (figure 1).

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"OPLS offers enhanced visualization when there is a large amount of Y-orthogonal structure in X."

"Whereas both methods divide the variability in a dataset into systematic (structured) and residual (noise) – OPLS further splits the systematic variability into two components: predictive (everything correlated with the response, Y); and orthogonal (everything not correlated with the response)." We compared OPLS and PLS performance applied to cell culture Raman data.

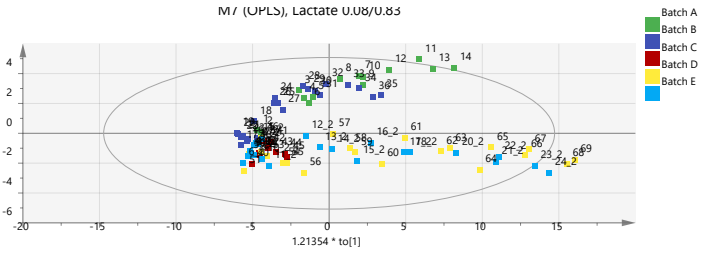

Figure 1. *The result: OPLS allowed for clearer pattern identification, improving the ability to distinguish between within and between batch variability. The OPLS method also helped with the interpretation of signals in Raman spectra that correlated with batch trends.*

Kaiser obtained the Raman data using a RamanRxn2TM-785 to monitor five CHO cell culture batches in situ, with samples collected at least daily for off-line analysis. Off-line data were matched to in-line Raman spectra. Among the parameters of interest were various metabolites, including lactate.

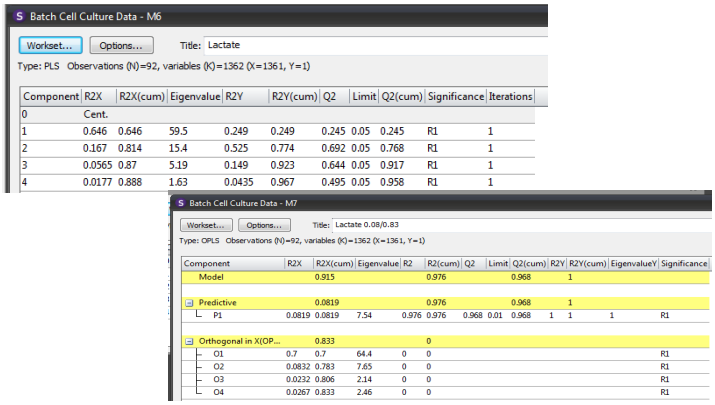

Figure 2. *shows an overview of the lactate PLS/OPLS model, comparing the two model options to analyze the same Raman dataset, and illustrating the breakdown of predictive vs orthogonal systematic information with OPLS. In this case the OPLS model yielded clearer patterns in the data and more visibly defined the batch-to-batch variability. In this case of R2X(cum) 0.08 predictive/0.83 orthogonal the OPLS yielded clearer pattern.*

The customer:

Kaiser Optical Systems, Inc., a leading manufacturer of Raman spectroscopy solutions.

The challenge:

Visualize batch-to-batch variability using Raman spectroscopy data from a cell culture process.

The solution:

Compare the effectiveness of OPLS and PLS, two multivariate methods available in SIMCA, through application on a Raman dataset acquired by in-line process monitoring of a cell culture process.

The result:

OPLS allowed for clearer pattern identification in the dataset, improving the ability to distinguish between within and between batch variability. The OPLS method also helped with the interpretation of signals in the Raman spectra that correlated with batch trends.

SIMCA®-Q solution from Sartorius Data Analytics

SIMCA-Q embedded solution delivers real-time process monitoring that ensures product quality. SIMCA-Q is part of the Umetrics® Suite of Data Analytics Solutions, a family of proven data analytics solutions that work seamlessly together.

Sartorius Data Analytics AB

Phone: +46 40 664 25 80
E-mail: umetrics@sartorius.com

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