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Application Note

Multivariate Batch Control (SIMCA-control)

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Batch Control

SIMCA-control is a model predictive control (MPC) method integrated with the multivariate modeling techniques utilized in Umetrics' SIMCA software. There are two forms of batch control included in SIMCA-control, observation level (batch evolution control, BEC) and batch level control (BLC). The objective of BEC is to find the set of manipulated variables (X_{MV}) that maintain the process on a defined trajectory. An example may include the adjustment of nutrient flow so that a BE score value is maintained within SPC limits. BEC is a regulatory type of control executed at a relatively high frequency.

For batch level control (BLC) the goal is to find the set of X_{MV} that result in optimized final batch conditions. An example may include adjustment of nutrient levels to maximize yield at the end of fermentation. Batch level control is a supervisory type of control that is only executed at selected times for mid- course type correction.

These two methods may be paired in a cascade configuration to provide both regulatory (frequent adjustments to keep the process in-control) and supervisory (mid-course correction) control of final qualities. As an example, in cell culture fermentation BEC is used for adjustment of nutrient addition to maintain cell performance along a desired trajectory while BLC may be used to adjust the desired cell performance trajectory in order to optimize the yield at batch completion (Figure 1).

Monitoring and control

N SIMCA-online is used in many industries for monitoring batch systems. With the predictive capabilities of SIMCA-control, monitoring is enhanced by providing reliable predictions of future process performance. Figure 2 depicts an example BE control chart containing the information presently provided

in SIMCA-online including the measured process up to the current maturity (black), the model average (green) and +/- 3 control limits (red). With SIMCA-control these control charts may also include the desired trajectory (green dashed) as well as open loop[1] (red dashed) and closed loop[2] (blue dashed) predicted trajectories.

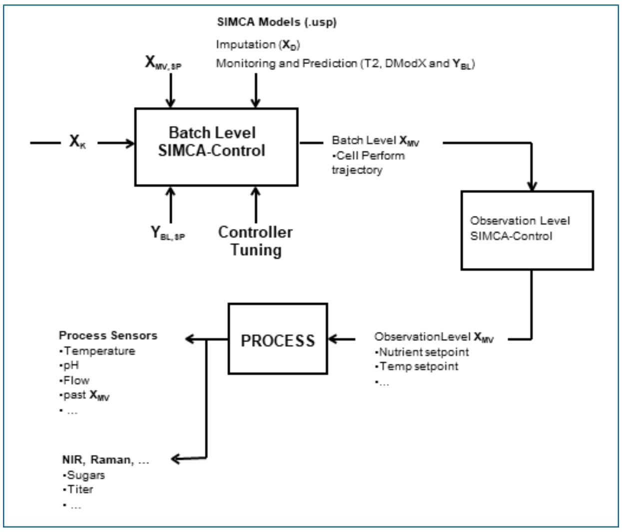

Figure 2 Schematic of a cascade control configuration

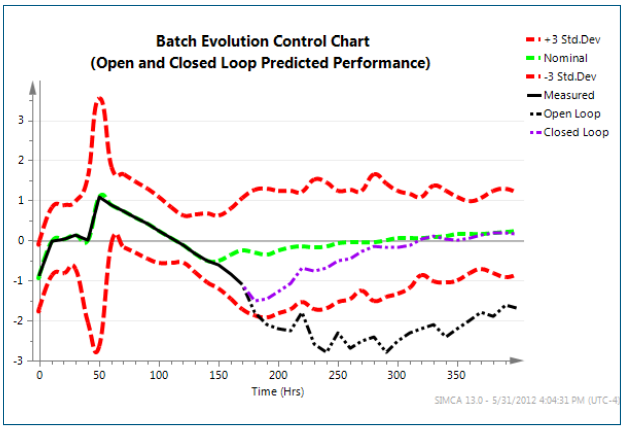

Figure 1 Observation level control chart for score or process variable

At the batch level, SIMCA-control provides open and closed loop predictions of final batch conditions (predicted qualities and yield) and the typical multivariate control charts (Figure 3).

[1] *Open loop refers to the predicted trajectory of the process if no process adjustments are implemented.*

[2] *Closed loop refers to the predicted trajectory of the process if the adjustments from SIMCA-control are implemented*

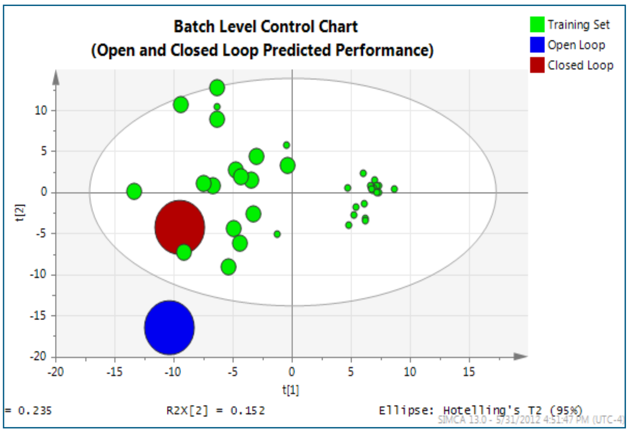

Figure 3 Batch level control chart showing predicted open and closed loop final batch performance

Control objective (Model Predictive Control)

Model predictive control (MPC) is a technique where adjustments to a process are selected by finding the set of manipulated variables (**X_{MV}**) that result in optimal process performance. Traditionally only process outputs (**Y**) are considered in the objective. With SIMCA-control, multivariate terms are integrated into the objective to assure adjustments made by the controller are constrained to the knowledge space. This is especially important for regulated industries, such as pharmaceutical and biologics, where a process must be shown to operate within regions that assure good quality product (design space).

A multi-objective function is used to define process performance. The weights (θ) are used to adjust the control priority.

$$J = \theta_Y \{Error\ in\ Y\} + \theta_{T2} \{Error\ in\ T2\} + \theta_{DModX} \{Error\ in\ DModX\} + \theta_{XMV} \{Adjustment\ in\ XMV\}$$

The goal of the controller is to find operating parameters (**X_{MV}**) that;

- Provide desired qualities and yields (**Y**)
- Maintain the process within the knowledge or design space (Hotelling T2 and DModX)
- Keep the process close to a desired operating recipe (**X_{MV}**)

Benefits of SIMCA-control

SIMCA-control provides advanced control technology based on MPC methods. With the integration of multivariate modeling methods SIMCA-control offers many advantages over traditional MPC offerings including;

- Control of batch processes
  — Observation level regulatory control
  — Batch level supervisory control
- Design space control
  — Assure the process is maintained within T2 and DModX multivariate limits
- Advanced non-parsimonious modeling methods
  — Batch unfolding methods
  — PCA, PLS, OPLS, OPLS-DA
  — Data preprocessing (spectral, normalization, smoothing, filtering, etc.)
- Process Monitoring
  — Integration with industry leading SIMCA-online multivariate monitoring software