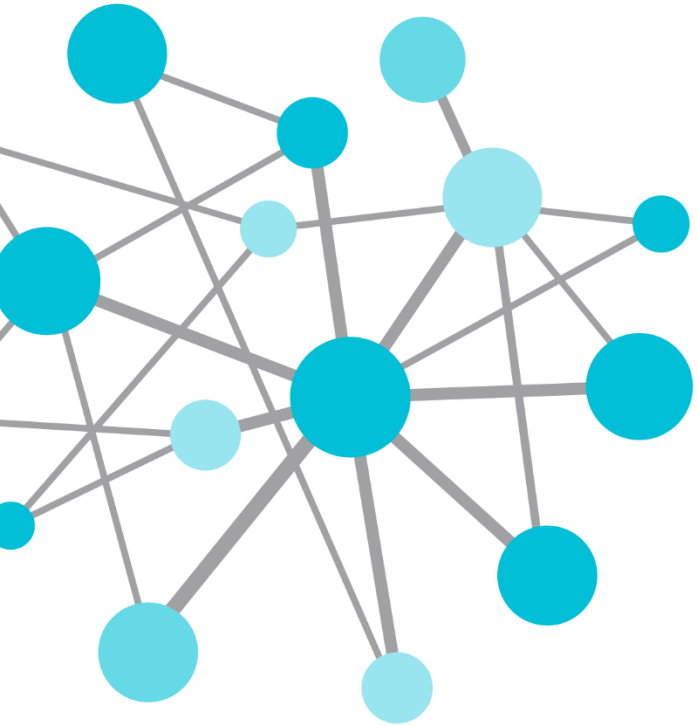

Value from Data -

Applying MVDA for real-time monitoring, prediction & control

Presented by Petter Moree – Umetrics

Domenic Schimizzi – Genentech

UMETRICS
AN MKS COMPANY

Genentech
A Member of the Roche Group

OSIsoft PI System with SIMCA-online in the Pilot Plant

"Access to model data and historical trends is invaluable as a monitoring and troubleshooting tool"

William McGreevy
Genentech, Inc.

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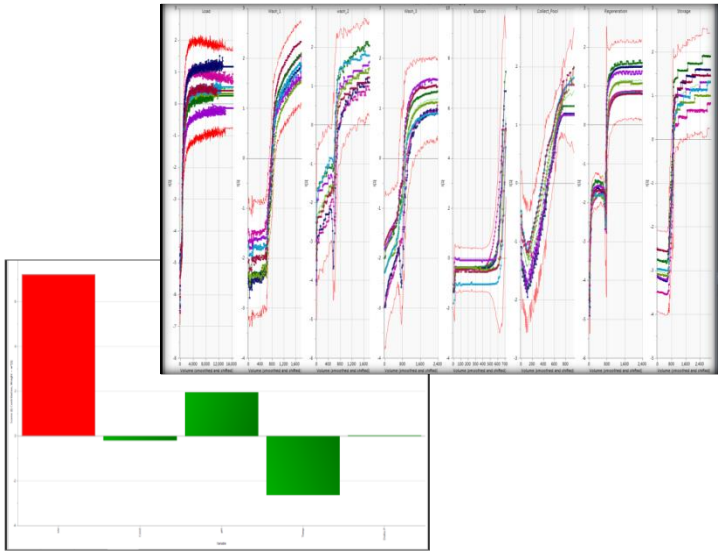


Business Challenge

- Genentech PD traditionally has relied on manual reviews for troubleshooting
- Reviews are subjective, reactive, time-consuming and require expertise

Solution

- The PD group implemented SIMCA-online using the PI System and PI Batch for online analysis of in-process chromatography at the pilot scale

Results and Benefits

- Enabled users in advanced analysis, troubleshooting and error detection
- Saved significant resources in manual reviews
- Increased process knowledge

Agenda

- What is MVDA?
- Values using MVDA.
  - PD & Pilot
  - Manufacturing
- Case Study: MVDA at Genentech
  - example from DSP in PD & Pilot
- Summary and Q&A

Umetrics - MKS Instruments

- Subsidiary of MKS Instruments
- MKS Instruments founded 1961 - Umetrics founded 1987
- 2400+ employees
- Global presence

Why Umetrics?

- World leading user friendly solutions for PAT and QbD
  - More than 700 leading companies & organizations
- World leading graphically driven software solutions
  - More than 7000 users
- World leading consulting, support and training services
  - More than 15000 individs educated
- Strong research cooperation with leading Chemometric research groups

MODDE®
For easier DOE and QbD

SIMCA®
Explore, analyze and interpret

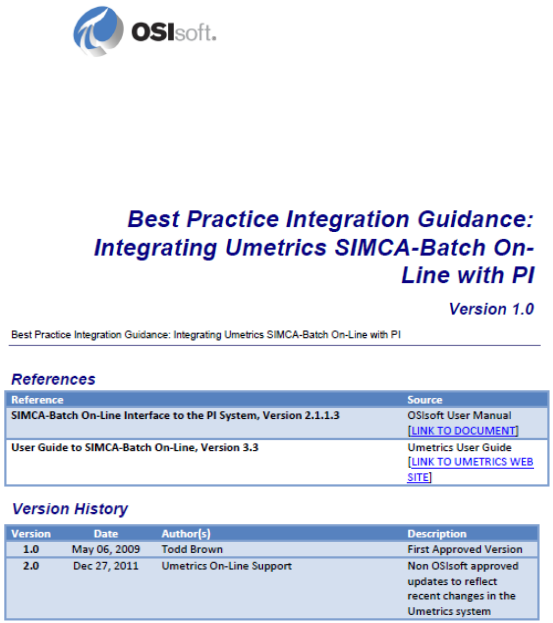
SIMCA-online®
For ensuring process quality

SIMCA-Q®
MODDE-Q®
For embedded OEM solutions

In-house training
Open courses

Why OSIsoft and Umetrics?

- Customer driven cooperation for more than 8+ years.
- More than 80% of Umetrics installation is based on the PI System as a fact the PI System offers an infrastructure fulfilling the needs and demands structuring batch data and metadata into one OTC solution.
- Large number of Use Cases and Success Stories presenting significant customer values by using the combined offering.
- Close collaboration in developing interfaces, documents, best practices and SOPs. Meetings on a regular basis between developers, product and marketing organizations from both parties.
- Joint Go-To-Customer approach when possible.



OSIsoft.

Best Practice Integration Guidance: Integrating Umetrics SIMCA-Batch On-Line with PI

Version 1.0

Best Practice Integration Guidance: Integrating Umetrics SIMCA-Batch On-Line with PI

References

Reference	Source
SIMCA-Batch On-Line Interface to the PI System, Version 2.1.1.3	OSIsoft User Manual [LINK TO DOCUMENT]
User Guide to SIMCA-Batch On-Line, Version 3.3	Umetrics User Guide [LINK TO UMETRICS WEB SITE]

Version History

Version	Date	Author(s)	Description
1.0	May 06, 2009	Todd Brown	First Approved Version
2.0	Dec 27, 2011	Umetrics On-Line Support	Non OSIsoft approved updates to reflect recent changes in the Umetrics system

SIMCA-online

With SIMCA-online , you have the power to monitor manufacturing evolution in real time providing quality information before the product is finished. SIMCA-online makes this possible using multivariate techniques combined with conventional SPC (Statistical Process Control), underpinned by a seamless graphical interface. Finally, you have the ability to react to quality issues as they happen.

SIMCA-OnLine BY UMETRICS

Average Overall Rating

★★★★★ (1 Reviews)

Write a Review

Contact Partner

Share on Twitter

Share on Facebook

Share on LinkedIn

Send as Email

Features & Benefits

- Increase manufacturing efficiency & quality using proven statistical methods
- Optimize process to reach desired quality target while reducing risk
- Very fast return on investment, often from the first major production deviation alert
- Provides information for engineering to make continuous improvements in the process

Industry

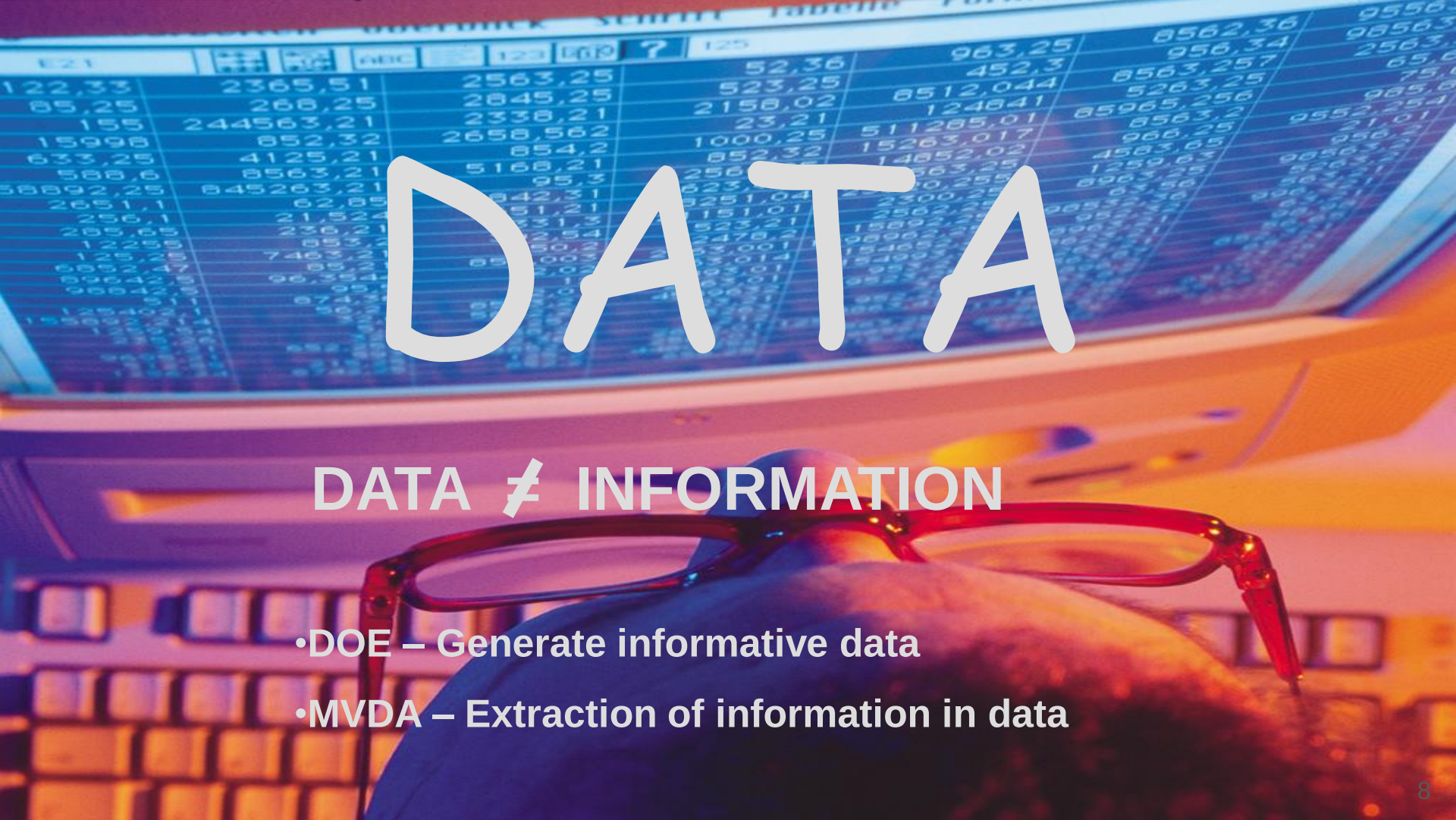
Oil & Gas
Chemical & Petrochemicals
Materials, Mines, Metals & Metallurgy
Pharmaceuticals, Food & Life Sciences
Pulp & Paper
Power & Utilities
Critical Facilities, Data Centers & IT

Solution Area

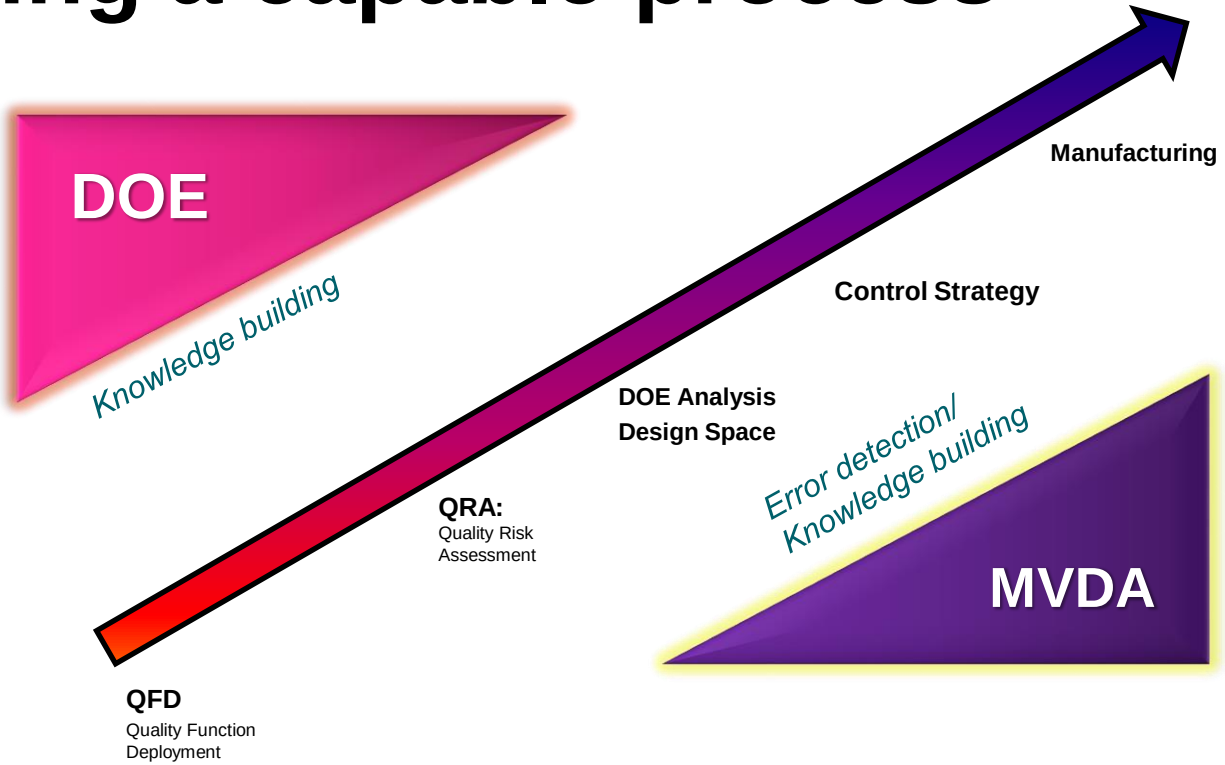
Process Characterization and Analytics
Process Control/Optimization
Visualization

Region Sold

Africa


DATA
DATA ≠ INFORMATION
•DOE – Generate informative data
•MVDA – Extraction of information in data

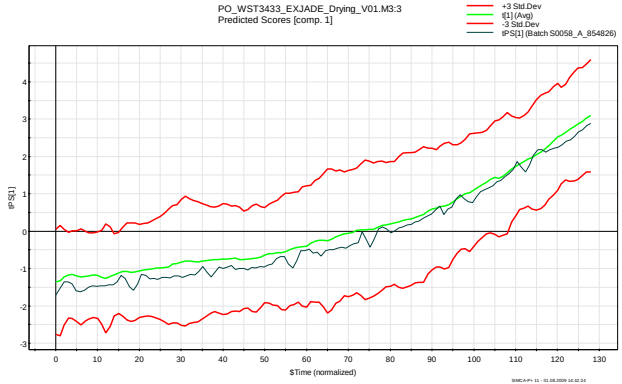
Building a capable process



Is this chart familiar?

DJIA = x1*Merck + x2*J&J + x3*Pfizer + x4*DuPont + ...

So this control chart is easy to understand....

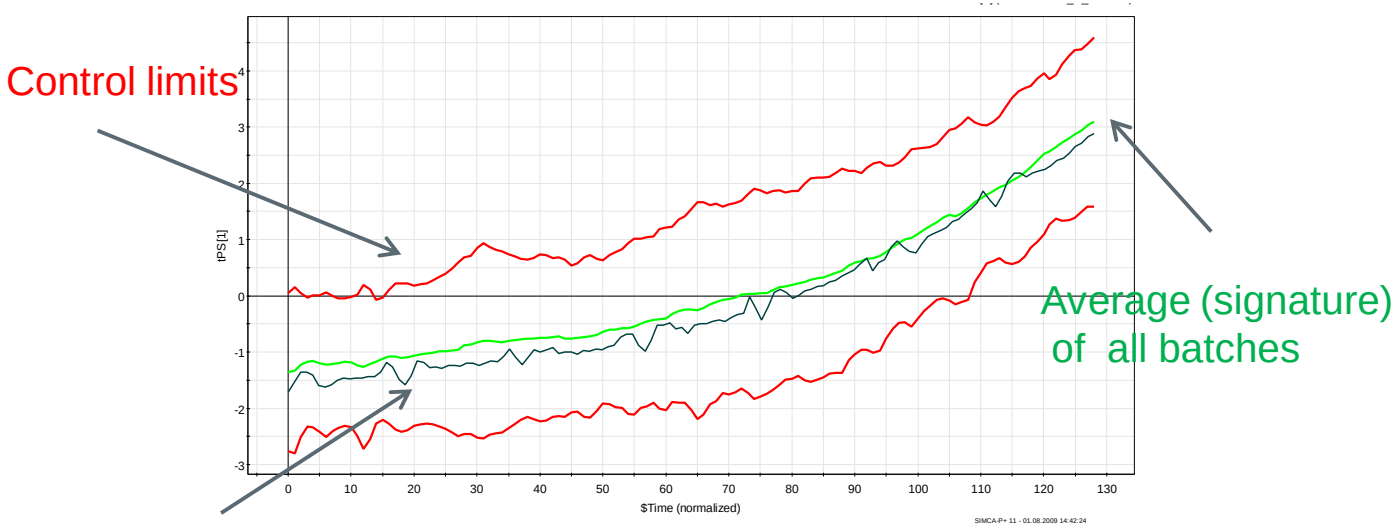


t_1= x1*Temperature + x2*Pressure + x3*Agitation speed + x4* pO2 ….

MSPC – Multivariate Statistical Process Control

Evolution Level – Monitoring

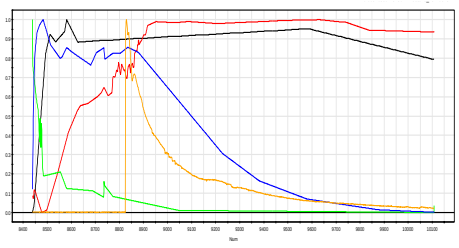
- Example of a fermentation

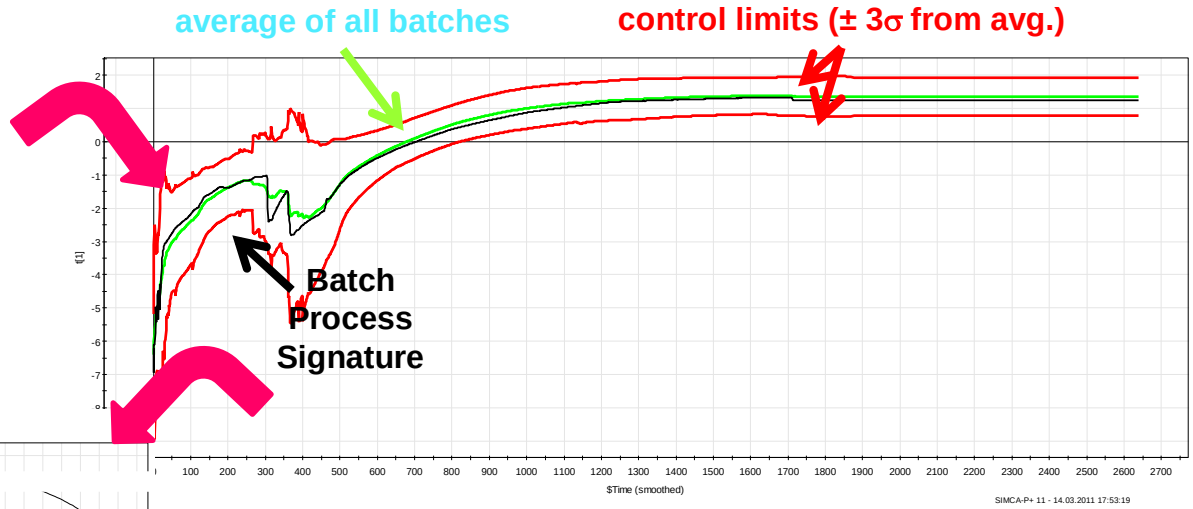


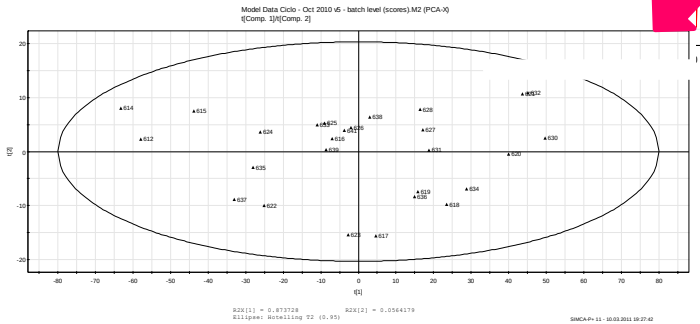
New batch assessed by the model

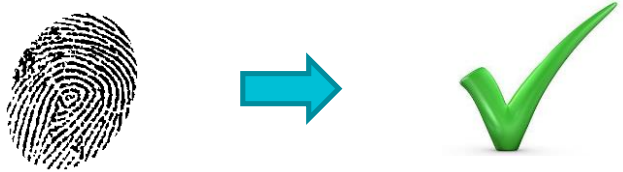
Statistical Process Control

BATCH CONTROL CHART









Role of Data analysis.

Objectives for the pharmaceutical & biopharmaceutical industry

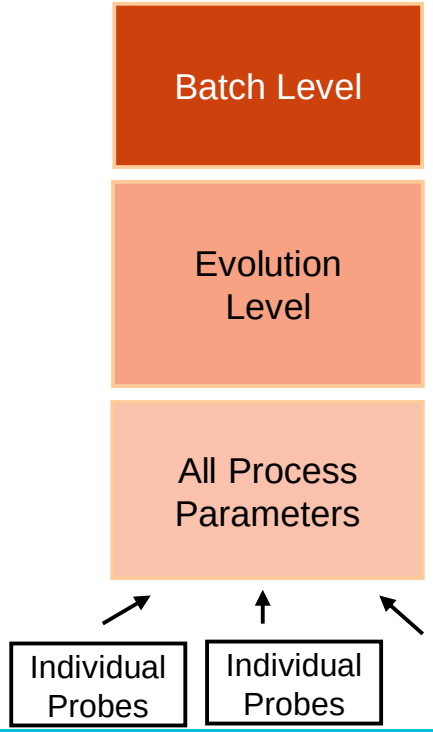
- Increase of **process understanding**
  - Identification of influential process parameters
  - Identification of correlation pattern among the process parameters
  - Generation of process signatures
  - Relationship between process parameters and quality attributes
- Increase of **process control**
  - Efficient on-line tool for
    - Multivariate statistical control (MSPC)
    - Analysis of process variability
  - Enabling on-line early fault detection
  - Support for time resolved design space verification
    - real time quality assurance
  - Predicting quality attributes based on process data
  - Excellent tool for root cause, trending analysis and visualization
  - Fundament for Continued Process Verification (CPV)

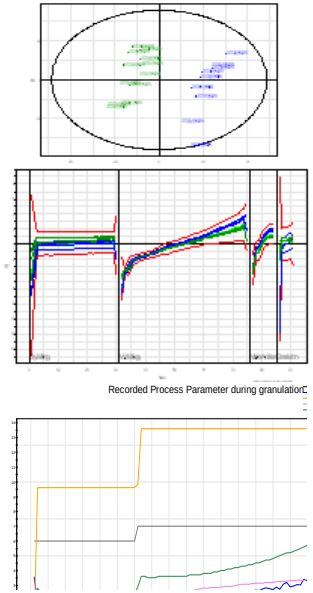
Development

Production

Work and Data flow

For Method Development



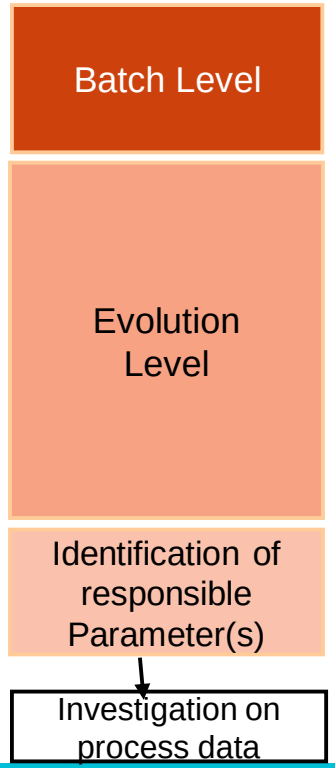


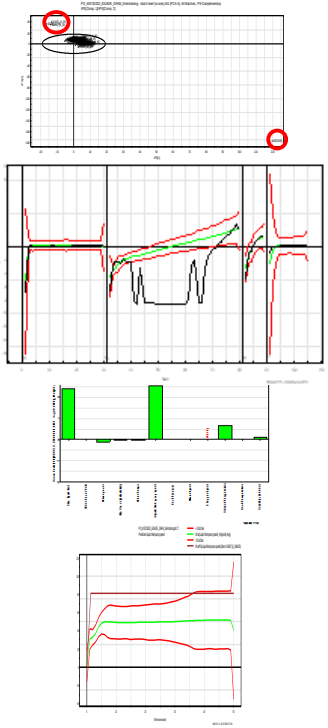
Reduction of Dimensionality

Aims:
- Creation of batch signature
- Identify correlation patterns
- Fundament for CPV

Work and Data flow

For Routine Use in Production





Aims:

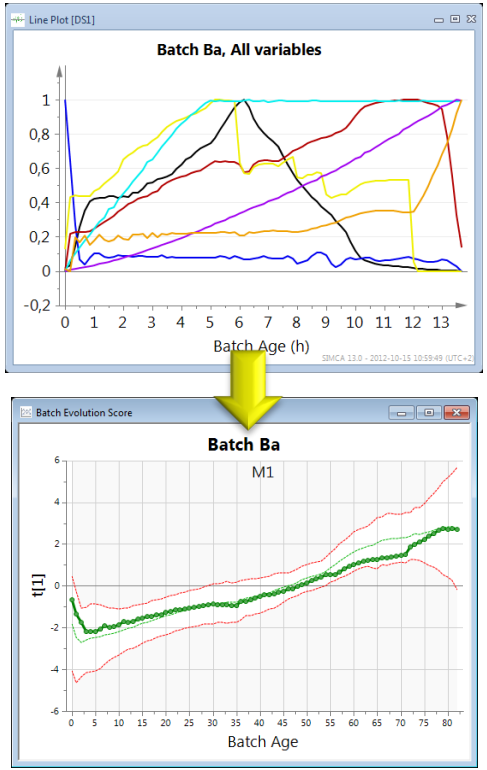
- Conformity check
- Real-time release testing
- Trend analysis
- Root cause analysis
- Early fault detection

Increased level of detail

Answers: What? When? How?

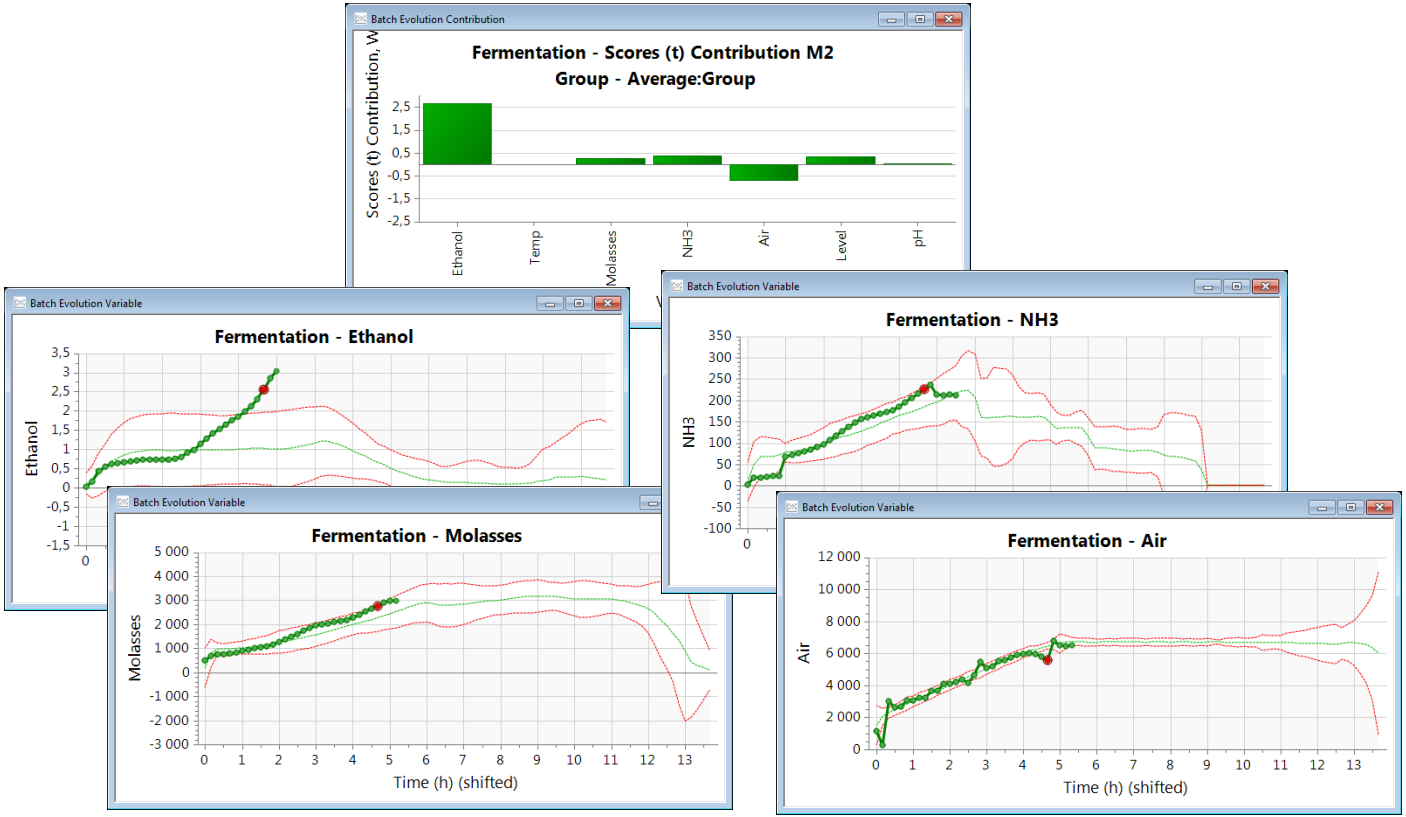
What makes Batch-SPC so powerful?

- The SIMCA product family uses a data compression technique
  - Multivariate data analysis
- Data from all relevant process parameters are concentrated to a few highly informative graphs
  - Simplifies overview, analysis and interpretation
  - Enable use of data by increasing ease of use
- Simple drill-down functionality to transfer compressed information back to raw data for analysis



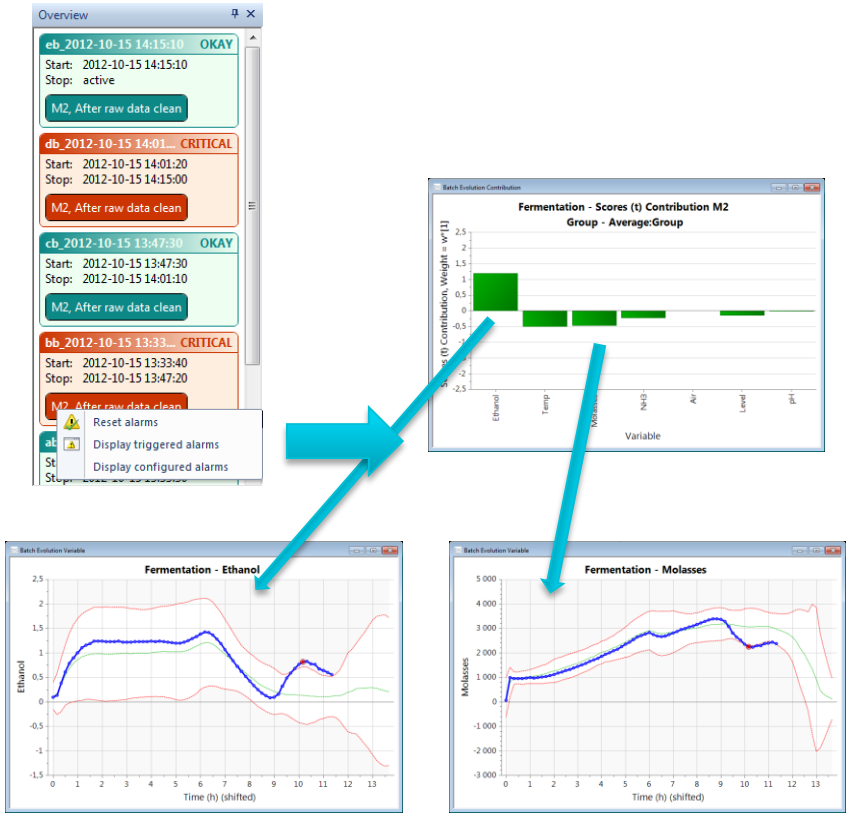
Drill-down for analysis

Full transparency, perfect interpretation



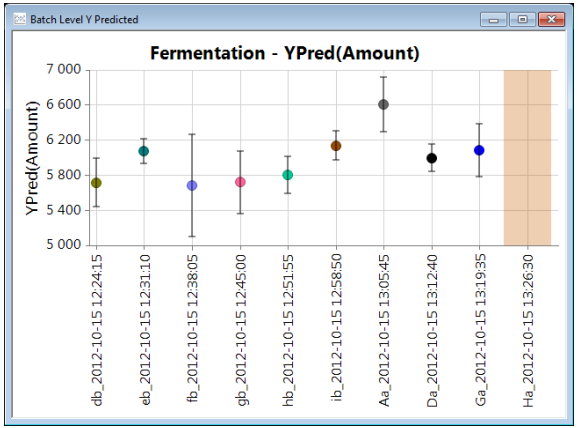
Monitor

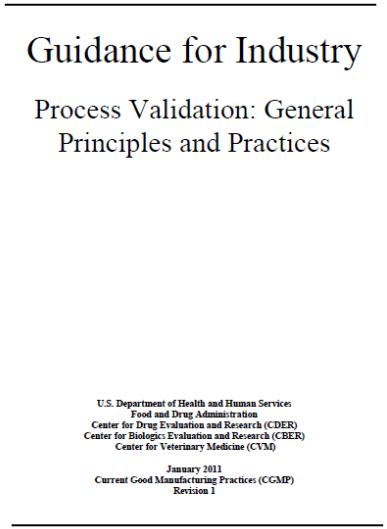
- Early fault detection
  - SIMCA-online technology is acknowledged for its ability to detect process issues before they become critical
- Project dashboard
  - Full drill-down to raw data for cause analysis
- Knowledge building
  - Instant analysis of process changes improves understanding
- Process visibility
  - Easy-to-grasp graphics makes the process status accessible to colleagues at all levels



Various objectives applying MVDA

- **Product quality information**
  - Indirect information based on process behavior
  - As long as a process behaves well, product should be according to specification
- **Soft sensor modeling**
  - Predict hard-to-get process properties from online process data, spectral data etc.
- **Predictive analytics**
  - Online prediction of product quality and properties
- **Continuoued Process Verification**
  - Ongoing assurance is gained during routine production that the process remains in a state of control.



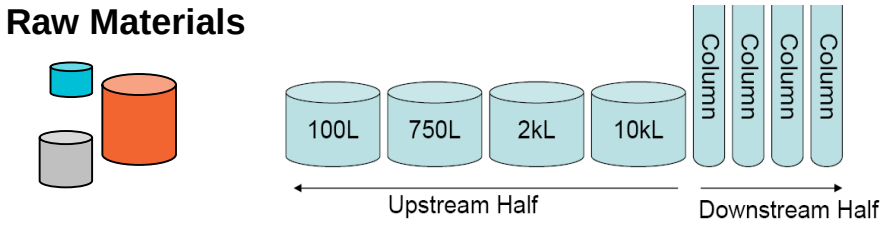

Guidance for Industry

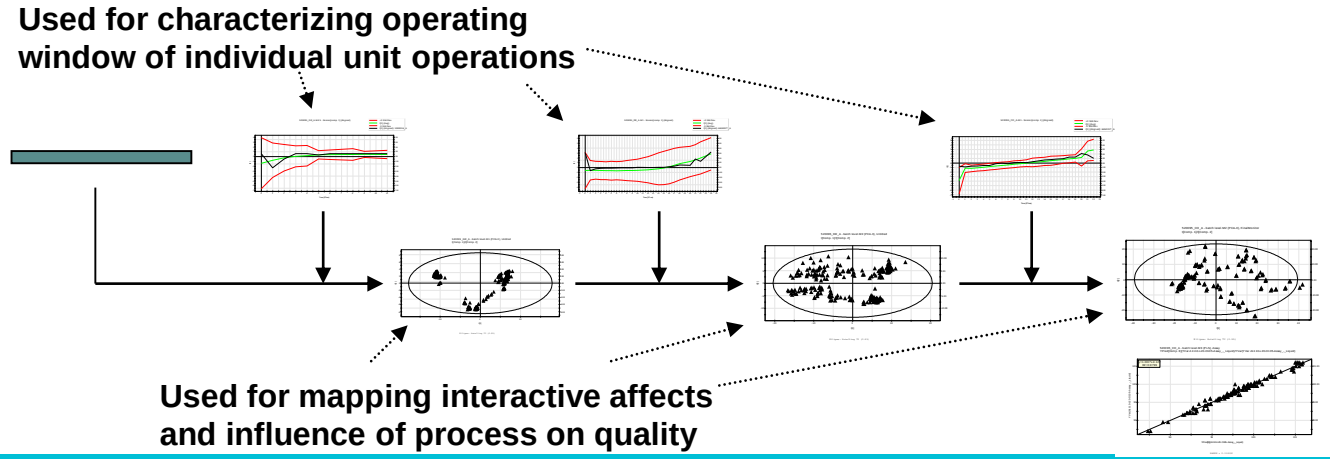
Process Validation: General Principles and Practices

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)

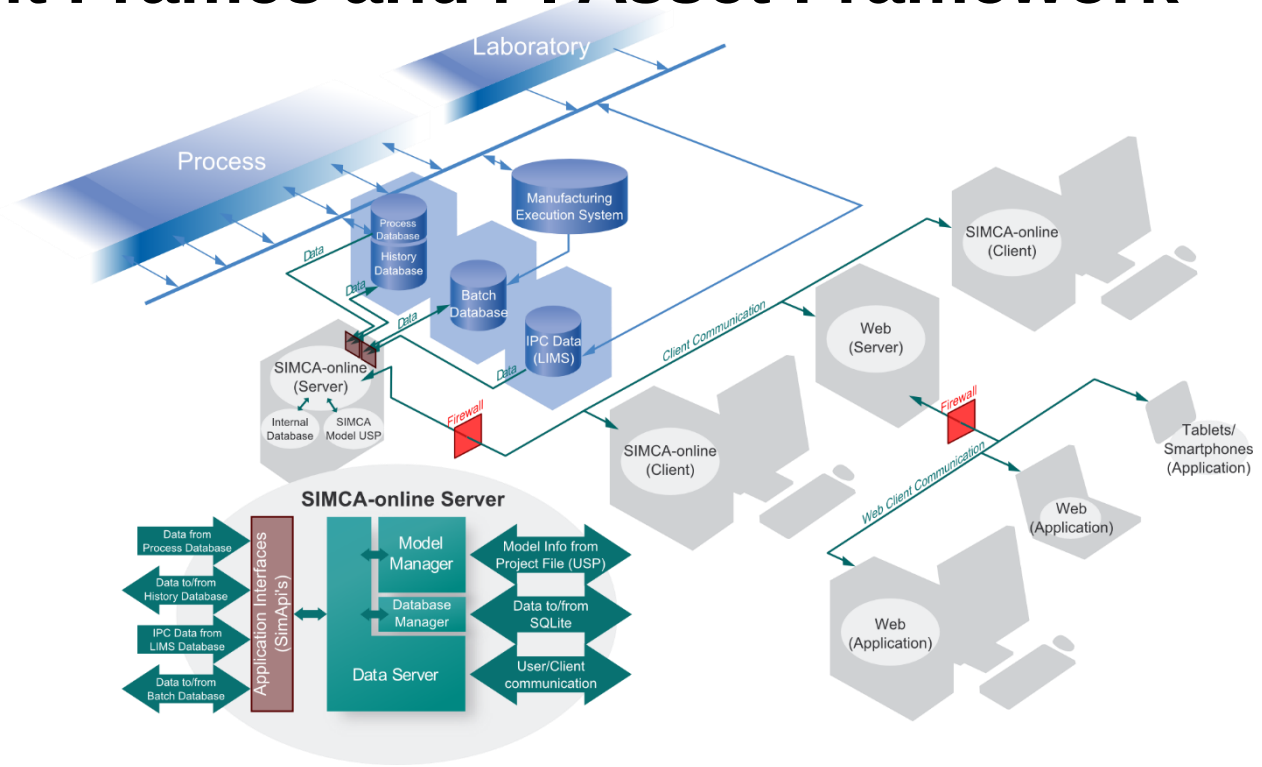
January 2011
Current Good Manufacturing Practices (CGMP)
Revision 1

Connecting process train





SIMCA-online with the PI System, PI Batch, PI Event Frames and PI Asset Framework



Genentech

- Member of the Roche Group
- Founded in 1976
- Research focused on oncology, immunology, neuroscience and infectious disease

OSIsoft PI System with SIMCA-online in the Pilot Plant

"Access to model data and historical trends is invaluable as a monitoring and troubleshooting tool"

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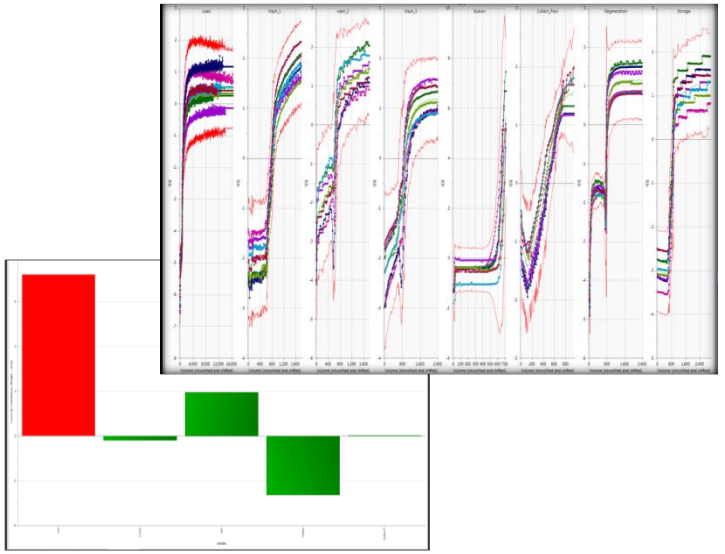


Business Challenge

- Genentech PD traditionally has relied on manual reviews for troubleshooting
- Reviews are subjective, reactive, time-consuming and require expertise

Solution

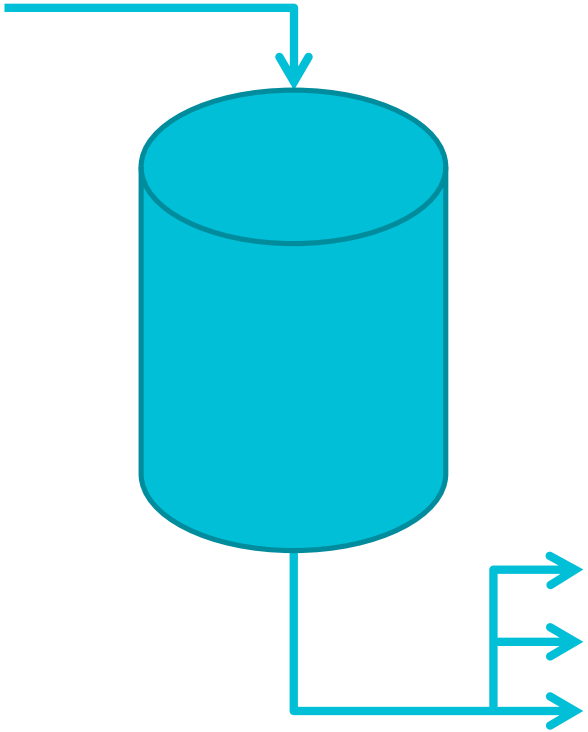
- The PD group implemented SIMCA-online using the PI System and PI Batch for online analysis of in-process chromatography at the pilot scale

Results and Benefits

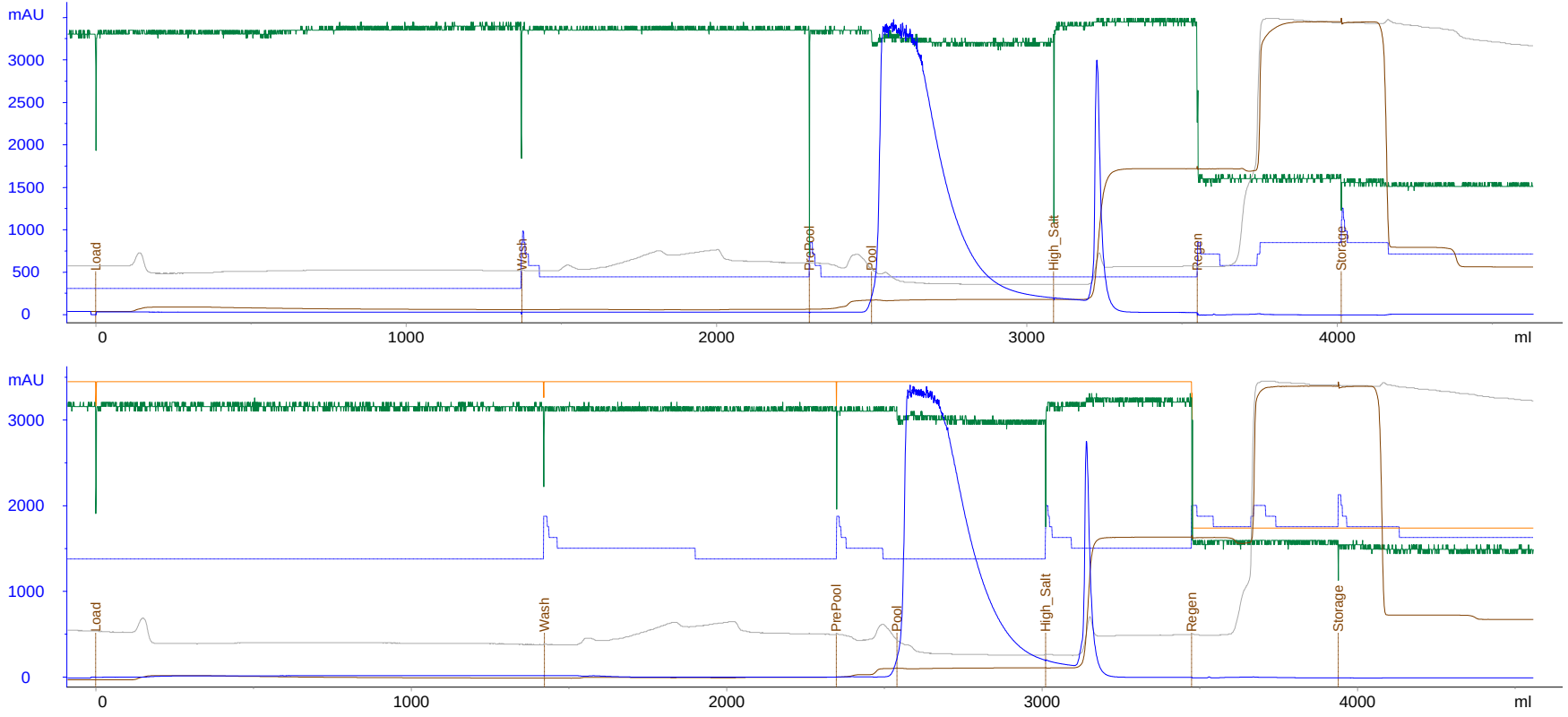
- Enabled users in advanced analysis, troubleshooting and error detection
- Saved significant resources in manual reviews
- Increased process knowledge

Column Chromatography

- Used to purify compounds on the relative speed at which they travel through a medium
- Medium can select for ions, antibodies, certain sized particles, etc.



Traditional Chromatogram Review

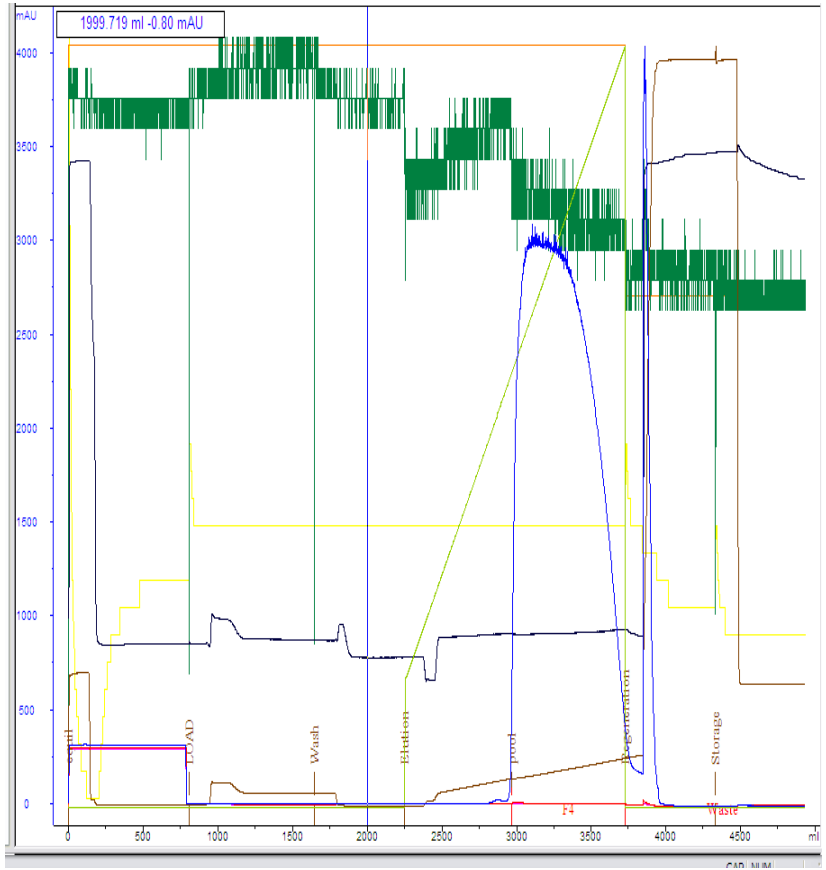


Problem Statement

- Chromatography reviews require in-depth expertise with many years of experience with the product family and the process
- Significant risk in a process that requires extensive on-the-job training with no quantifiable result
- Chromatogram reviews take resources that could be spent elsewhere

Project Objective

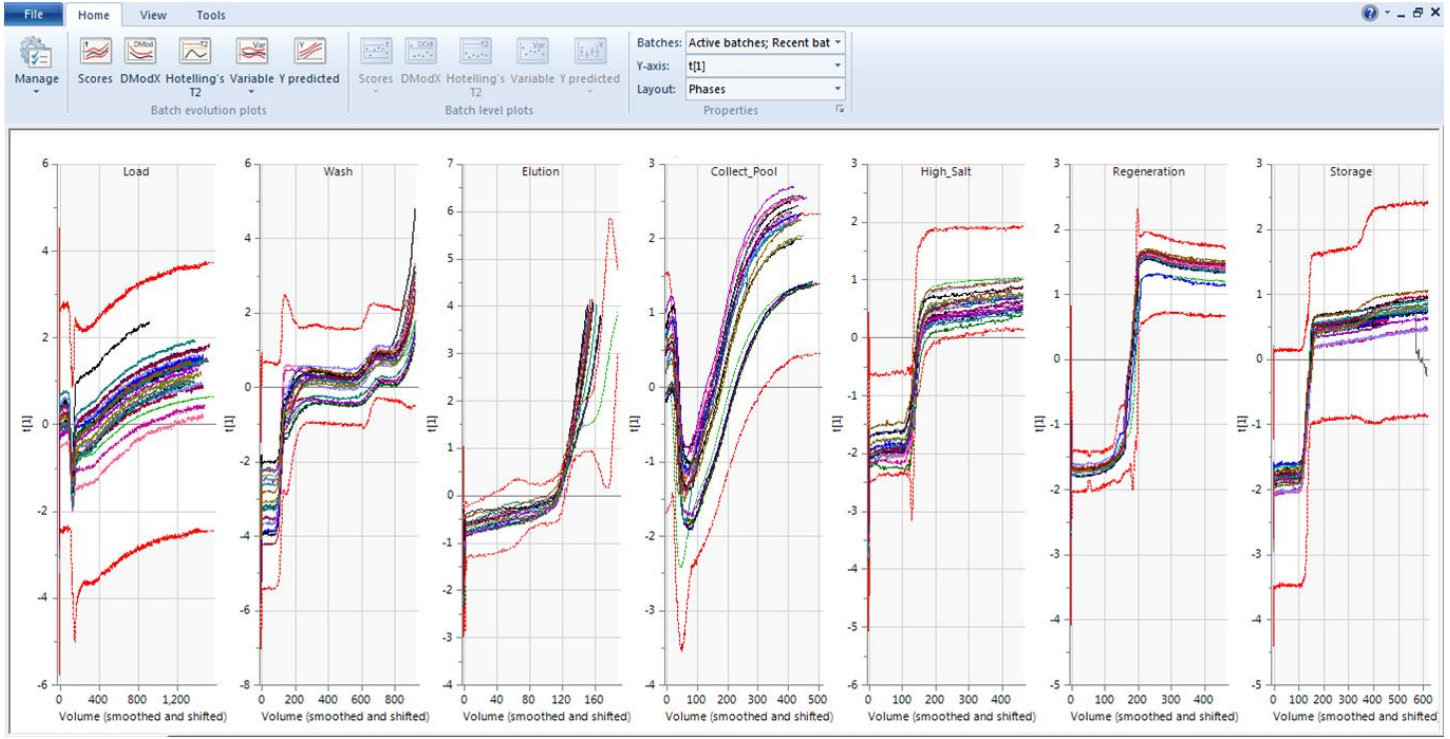
- Implement an automated chromatography review system to reduce labor, accelerate deviation detection and improve process knowledge



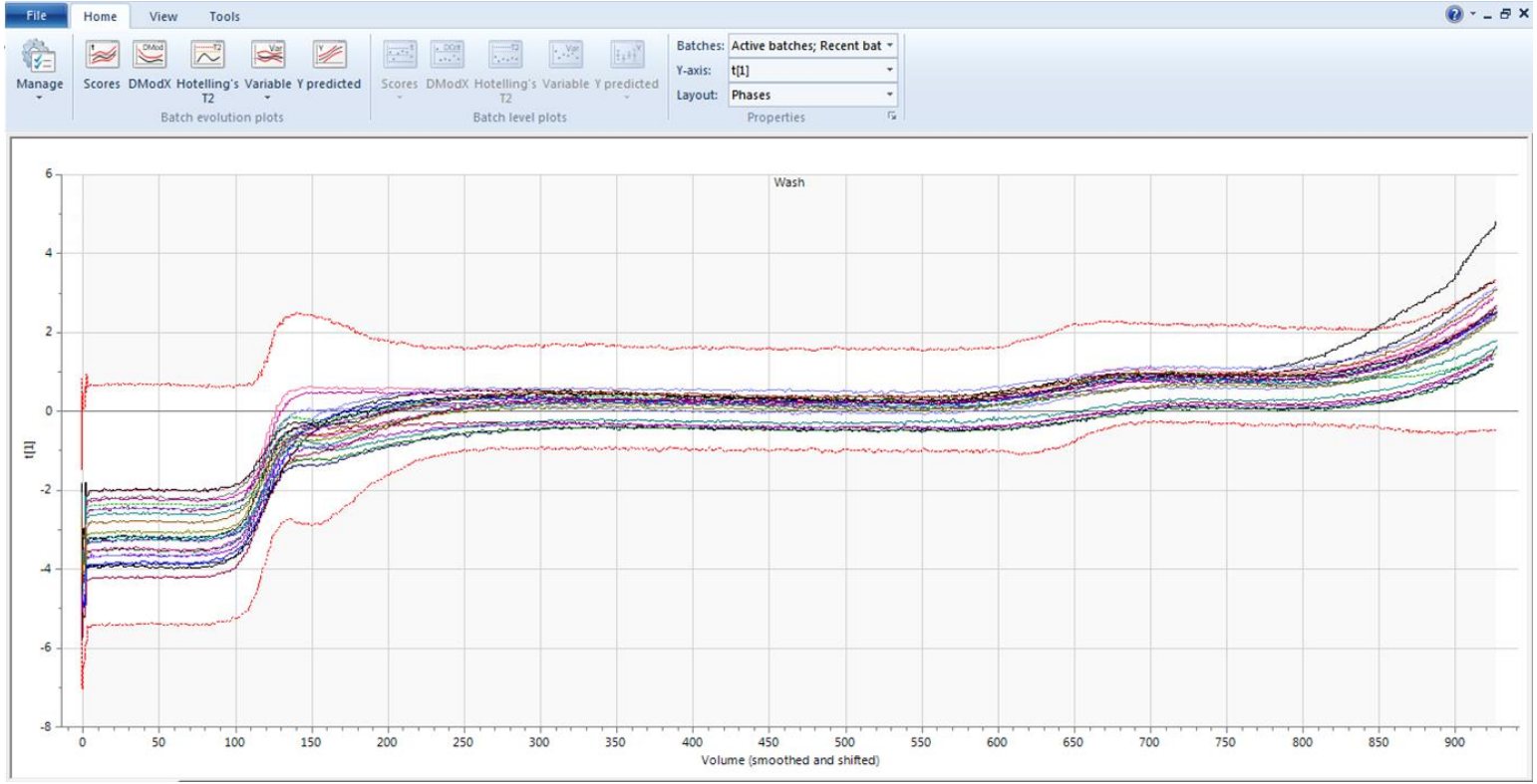
Batch Context and Model Development

- PI Batch configured in less than two hours on all units
- Other data historians have taken weeks of time to develop and configure batch context
- After initial MVDA model put online, batch data extracted from the PI System via SIMCA-online, accelerating model development

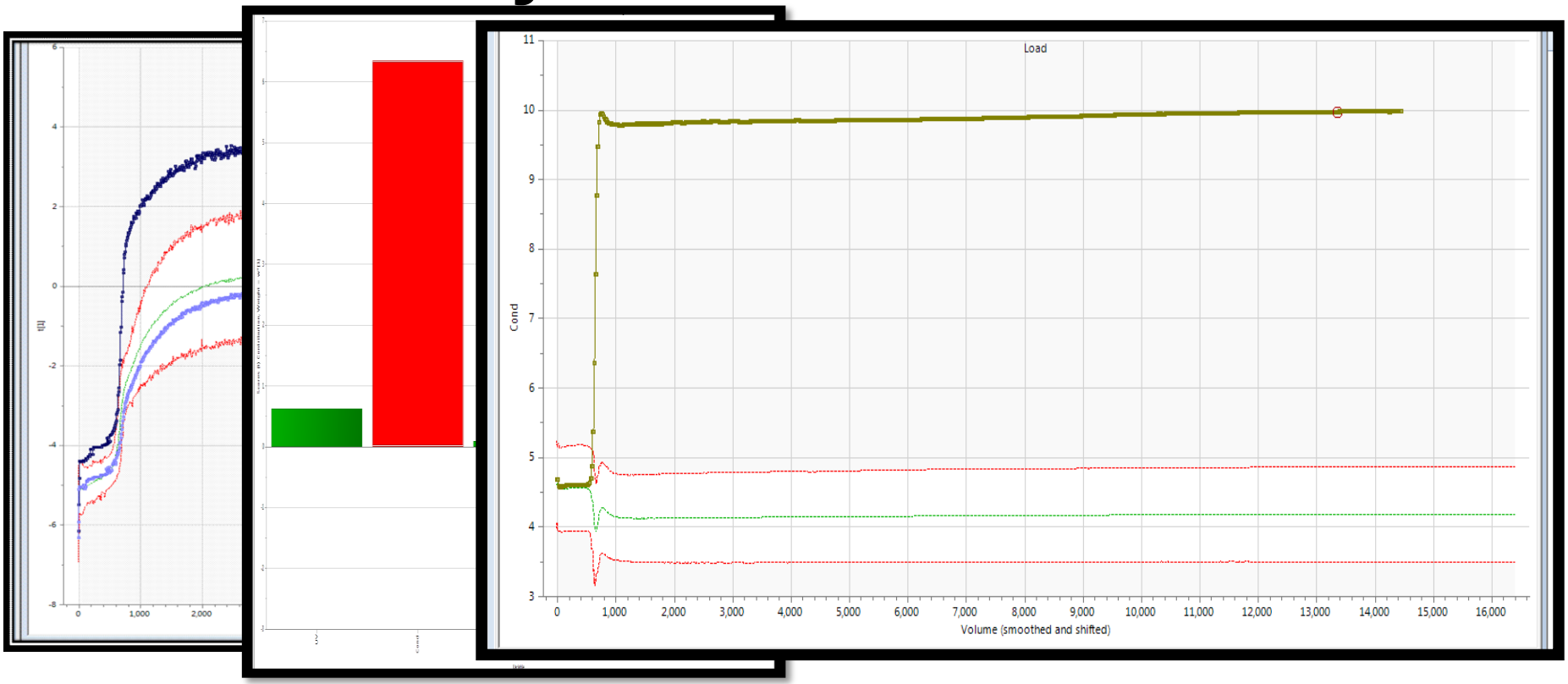
Batch Evolution for Chrom Process



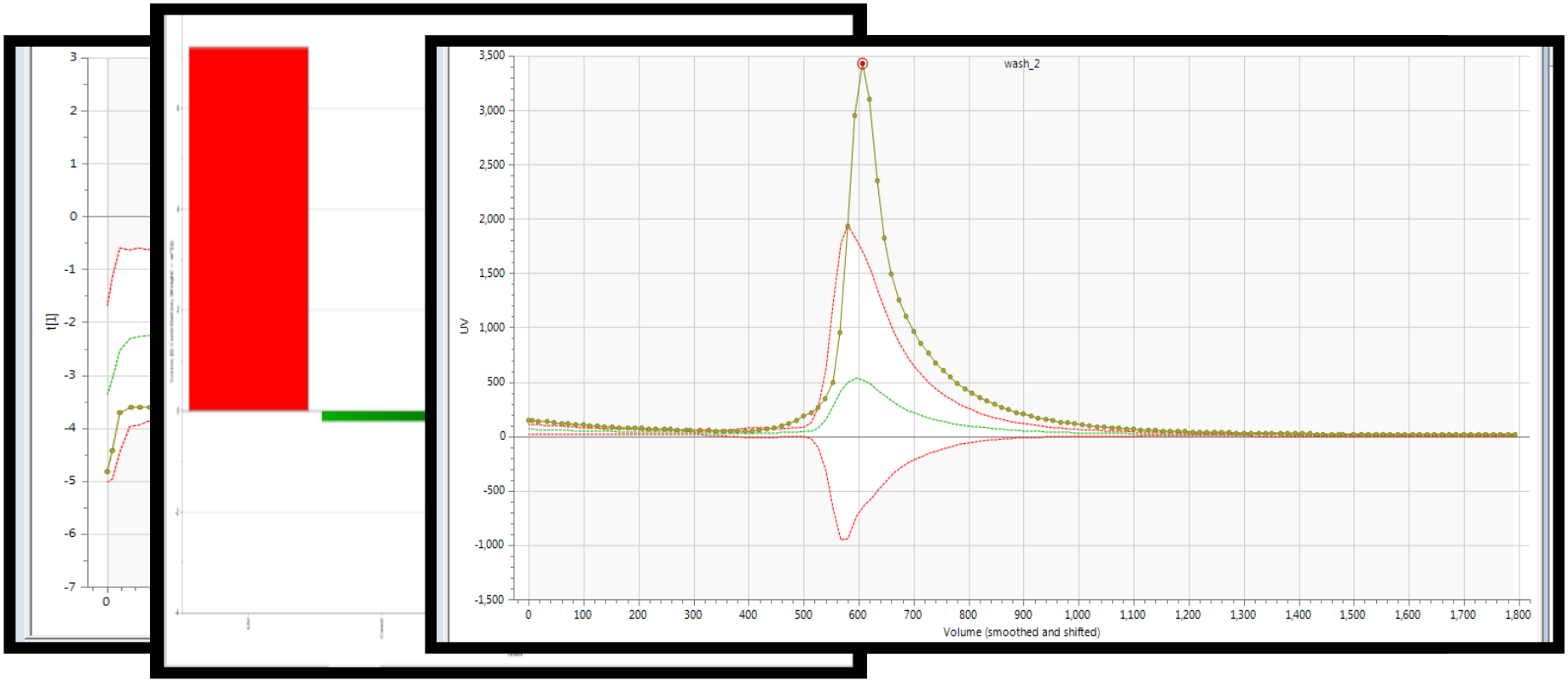
Batch Evolution in Single Chrom Step



Conductivity Deviation



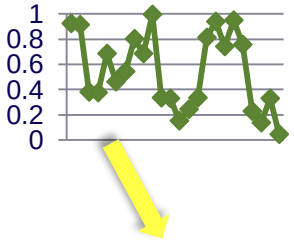
Abnormal Elution Peak



Motivation for QbD

- Reducing process variability is not necessarily desirable

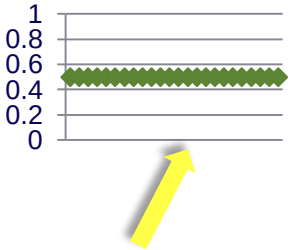
Input



With variation in inputs

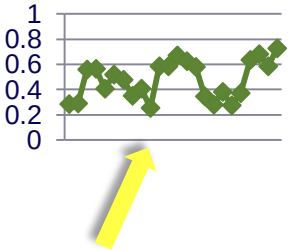
- Initial material qualities
- Environment
- Equipment

Process



Static process

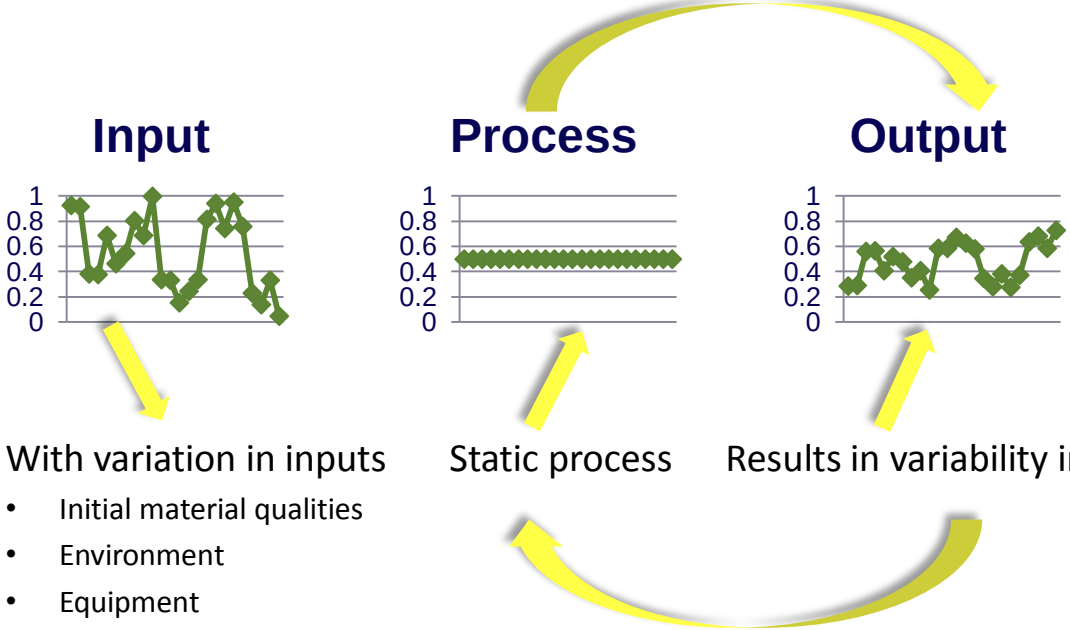
Output



Results in variability in outputs

Motivation for QbD

- Reducing process variability is not necessarily desirable



QbD and PAT Strategies

- Control strategy a) batch to batch control

Adjusting the process based on variations in the output

- Used in Semiconductor and other high throughput industries
- Affective if input variations are slow relative to the rate of production

QbD and PAT Strategies

- Control strategy b) feedforward control

Adjusting the process based on variations in the input

- Media and feed composition
- Used in pulp and paper and other industries with natural products with high variability

QbD and PAT Strategies

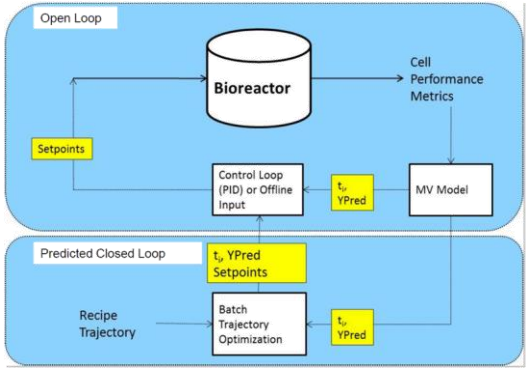
- Control strategy c) PAT control

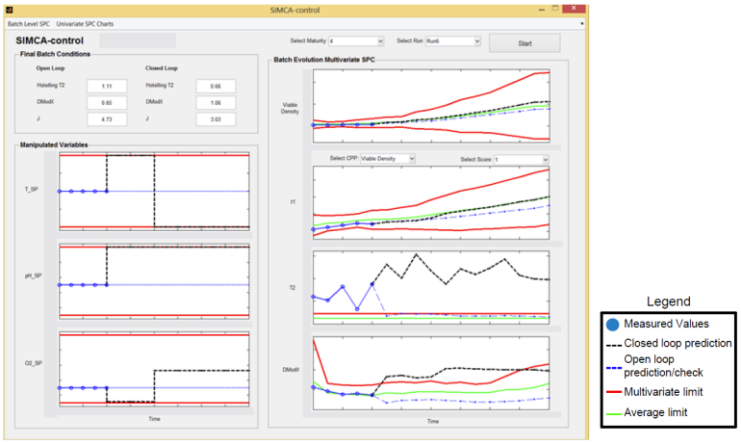
Adjusting the process based on measurement of quality in the process

- Used in many processing industries using various methods
  - Direct measurement of material quality
    Inferential control – estimation of quality from process measurements
    Spectral calibration

PAT control / SIMCA-control / SIMCA-online

Presented at IFPAC 2014



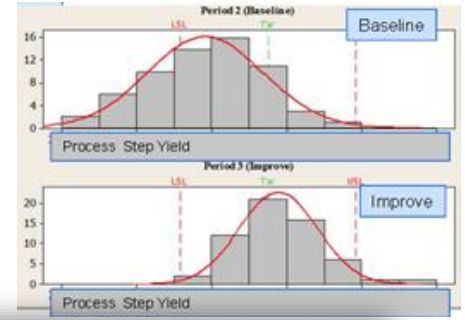


- Final day VCD improved on average 23% with SIMCA-control
  - 7 confirmation runs in parallel - open vs closed loop
- Improved robustness e.g. reduced variation in VCD, time etc.
- Harvest time decreased 20%

Lonza: Multivariate Online Batch modeling

- Lonza is a global company serving the needs of the pharmaceutical and specialty ingredients markets.
- Presented by Christine Bernegger / Head Program Management, February - Workshop der ISPE Affiliate D/A/CH

Lonza

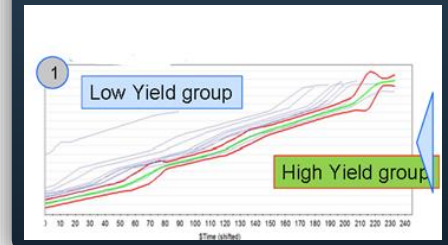


Customer Business Challenge

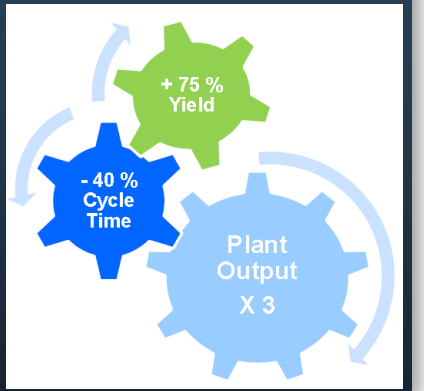
- Average Yield was lower than expected
- Variation in Yield gave a more difficult situation to plan work and delivery to end customer

Solution

Six sigma approach variability analysis for Yield optimization And Time Based MVA of On-line Process Parameters



Customer Results / Benefits



Amgen receive CIO 100 Award 2013

- “The new automated analytics system **saves time** and allows the team to **focus on the trends** instead of gathering and charting data. In one case, a yield issue was rectified in **less than a day** thanks to the new system; with Amgen’s old setup, it would not have become apparent for weeks.”
- “In one recent example, Amgen identified the cause of a cell culture problem about a month earlier than it otherwise might have. For that biologic product, making the fix early -and not losing that month- **saved $2.4 million**, she says. Depending on the product, manufacturing a lot can cost more than $1 million”, CIO Diana McKenzie says. **"This is Amgen's taming of big data**.“
- “Using statistical analysis of data points collected in **real-time** during the process, Amgen identifies "weak signals" that could indicate brewing problems in the manufacturing cycle. Scientists then delve deeper, taking corrective steps if necessary. The analytics system includes virtualized data warehousing tools from Denodo, multivariate analysis tools from **Umetrics** and various software modules from SAP.”

- Source: http://www.cio-asia.com/print-article/40347/

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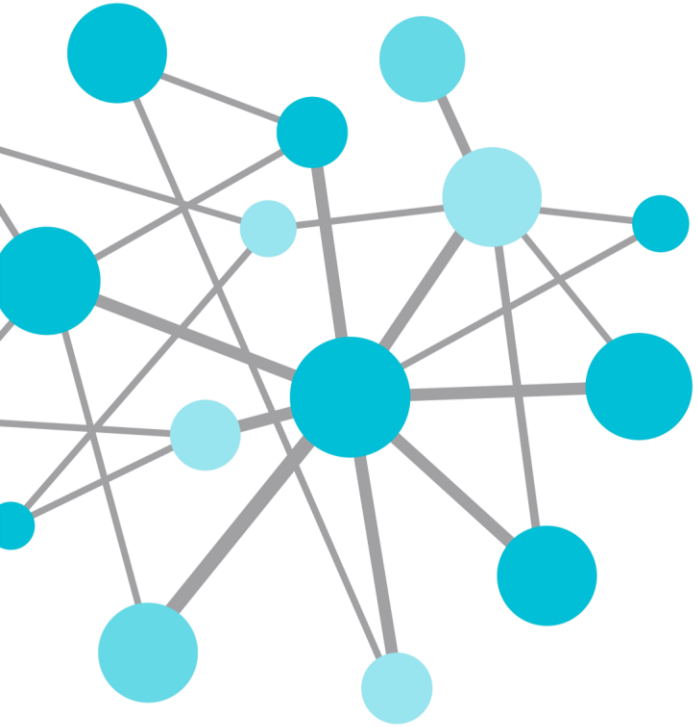

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