Use PI system and SIMCA online to build a Real-time Multivariate monitoring System

Phuong Vo
Anna Persson

Prometheus project

…. a journey to
Advance Process Control

Johnson & Johnson

Consumer

Medical Devices & Diagnostics

Pharmaceutical

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Pharmaceutical

Janssen In The World

At Janssen we work globally on the health of everyone

5,000
researchers
at various R&D centers

+ 37,000
employees
on a global scale

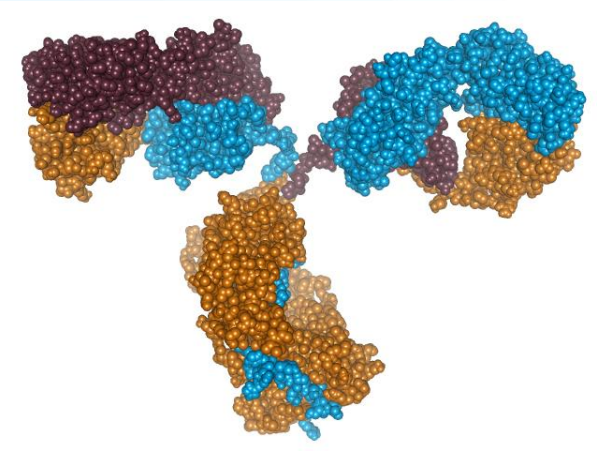
top10
fastest growing pharmaceutical company

15
new products
launched since 2009

33.5
billion USD
global turnover

6.9
billion USD
R&D investments in 2016

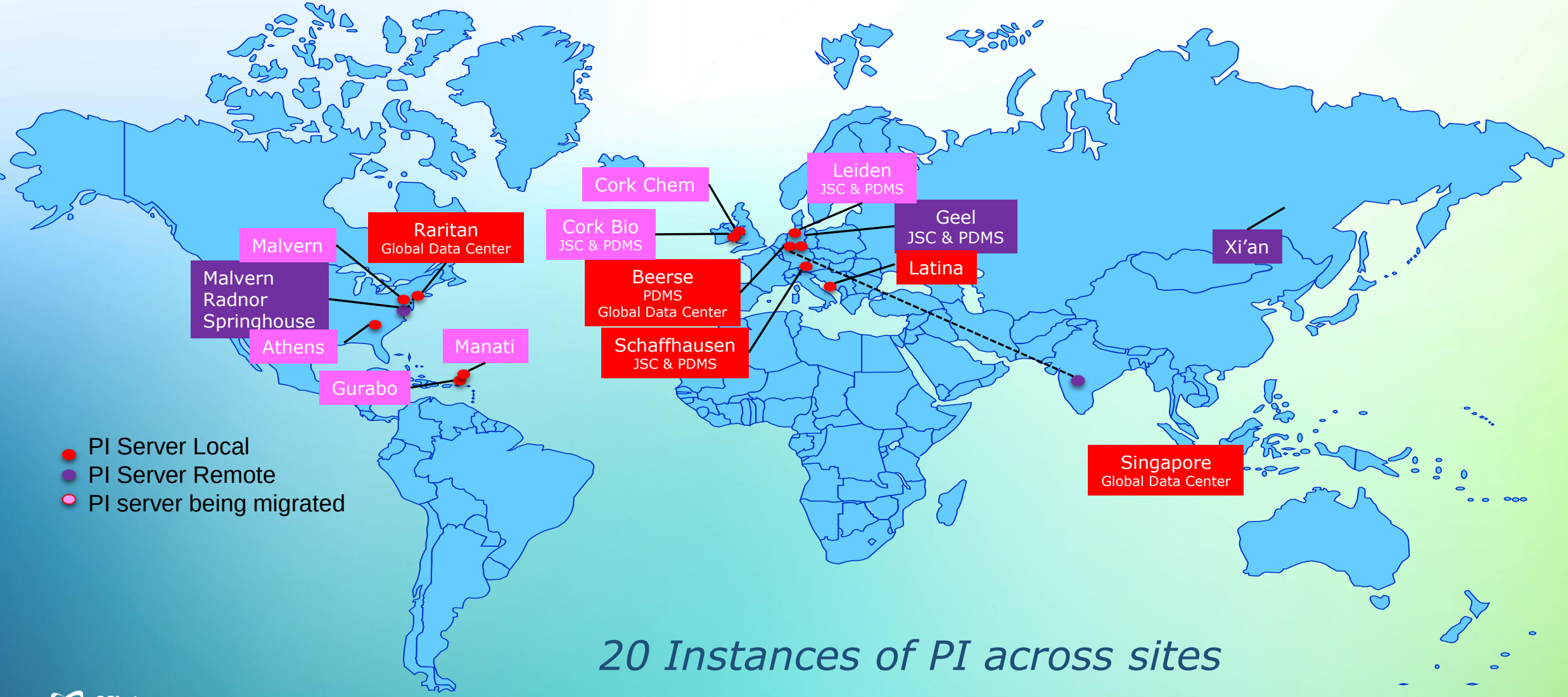
Janssen Biologics – The Netherlands



- ***Cardiovascular***
- ***Immunological disorder***
- ***Cancer***

> ***"We produce products that improve the quality of life of our patients, now and in the future"***

PI system Architecture Overview



20 Instances of PI across sites

Vision: Optimizing Global Deployment of PI system

Integrated Data Management

Continued Process Verification (CQA's and CPP's)

Efficiency (Batch Reporting & Automatic Data Capture)

One PI

One reliable source of integrated data, available anywhere, anytime, to anyone

Standardise

Enable

Implement

Globally

to add significa Business Value

Design to Value

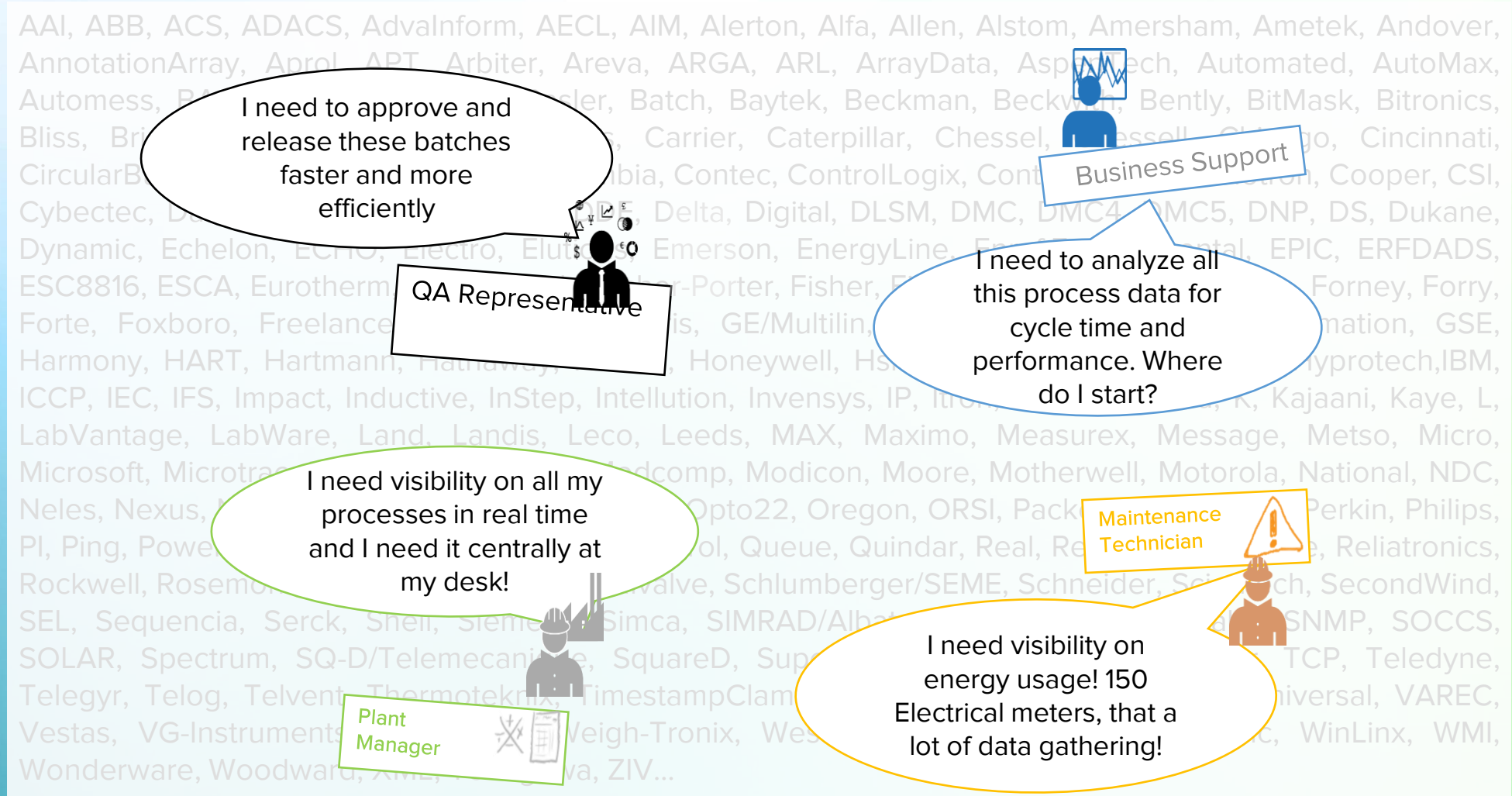
Real time Process Visualisation

Realtime process analytics

JSC RELIABILITY

CUSTOMER **COMPLIANCE** **COST**

Business Challenges



Business Challenges

General process flow of Monoclonal antibody production

Preculture

Fermentation

Direct Product Capture

Purification

Final testing

General process flow of Monoclonal antibody production

Preculture

Fermentation

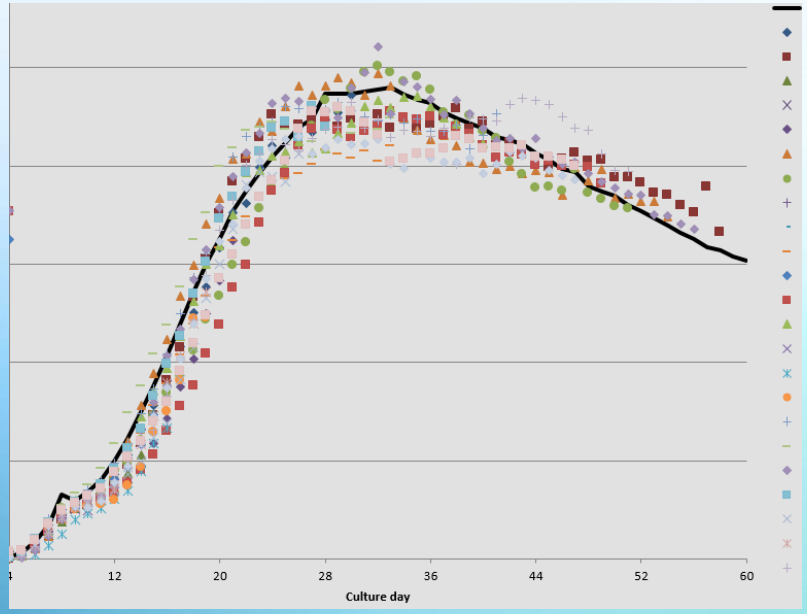
Purification

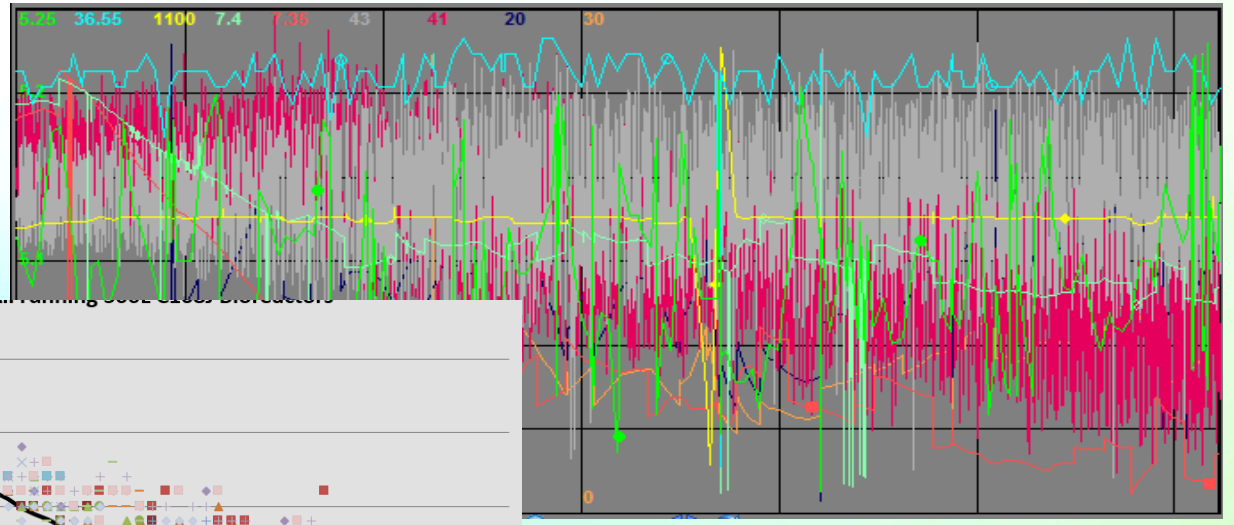
Final testing

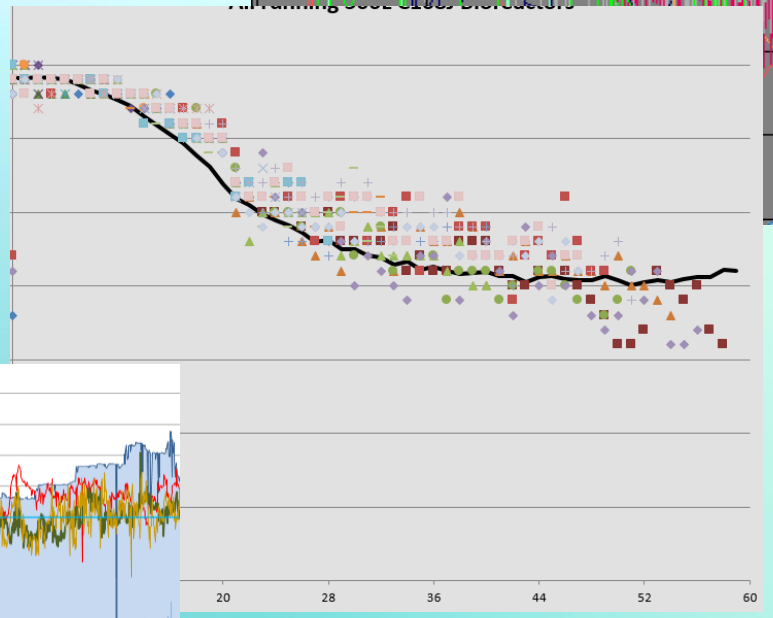
>50 parameters online

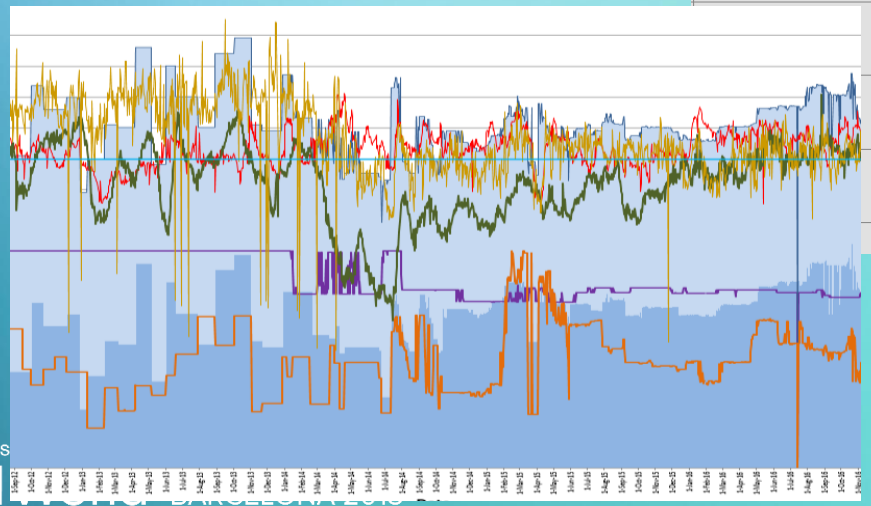
>15 parameters offline

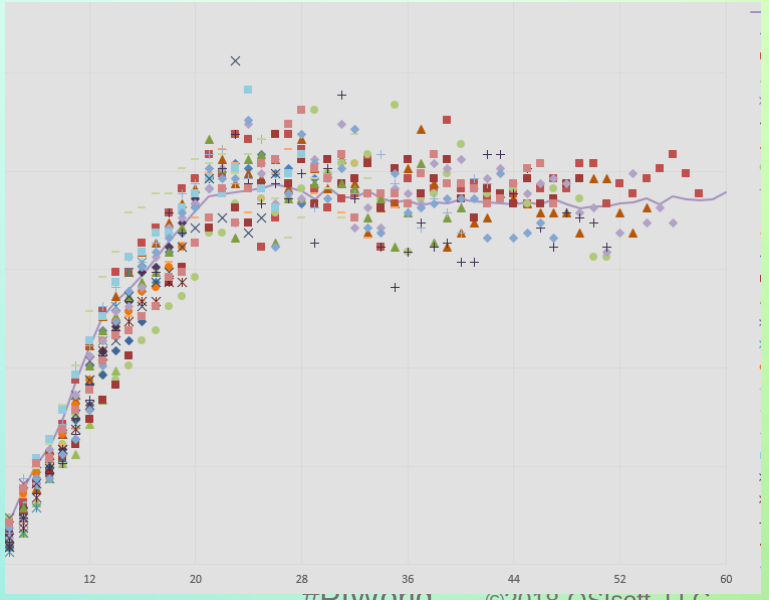
Current way of process monitoring



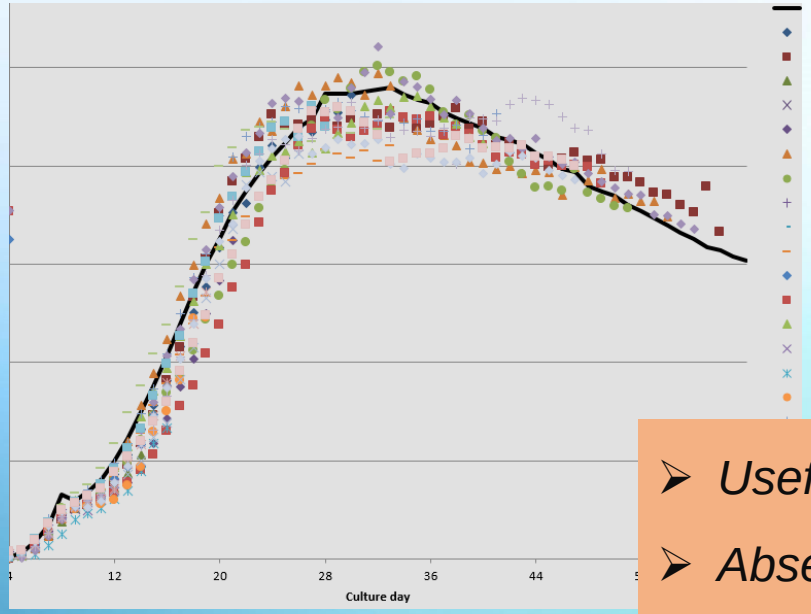


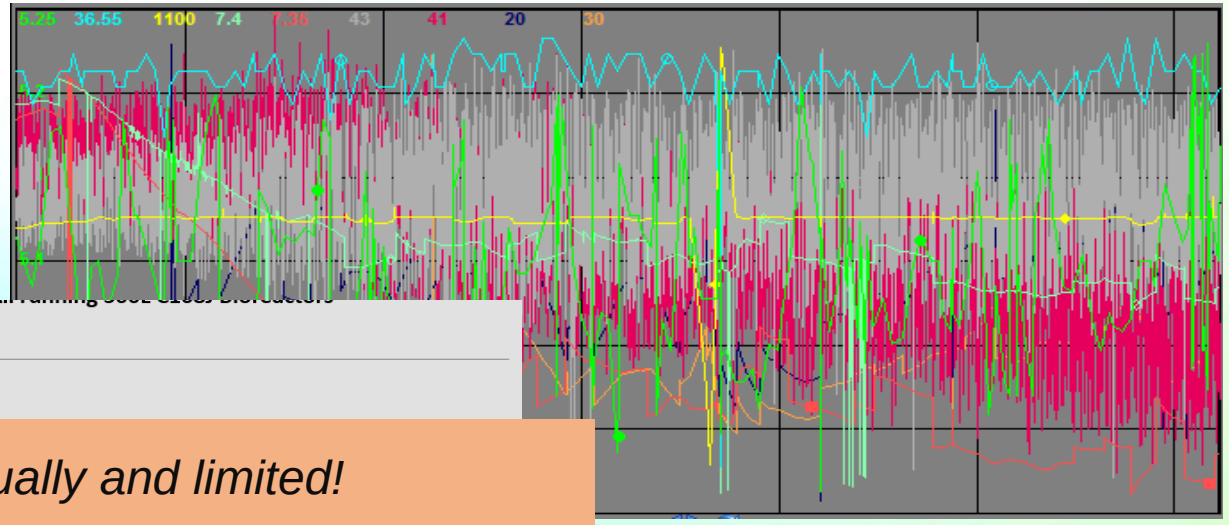


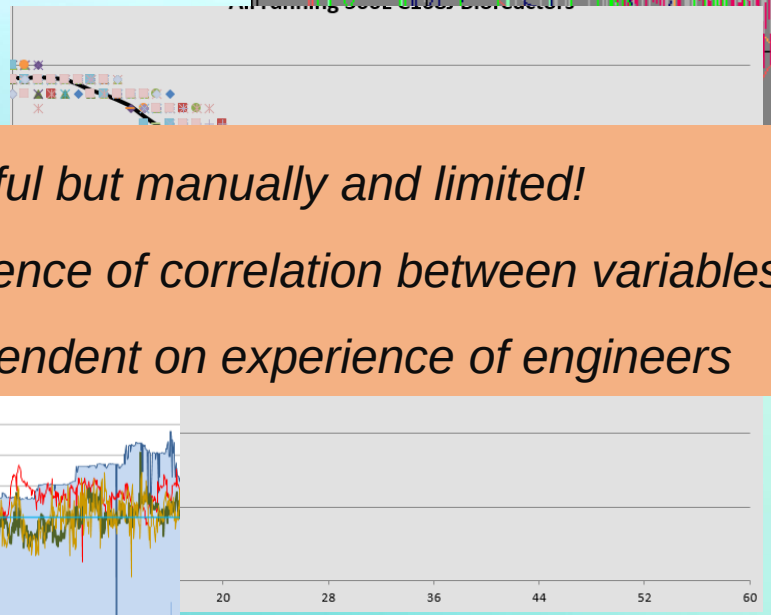




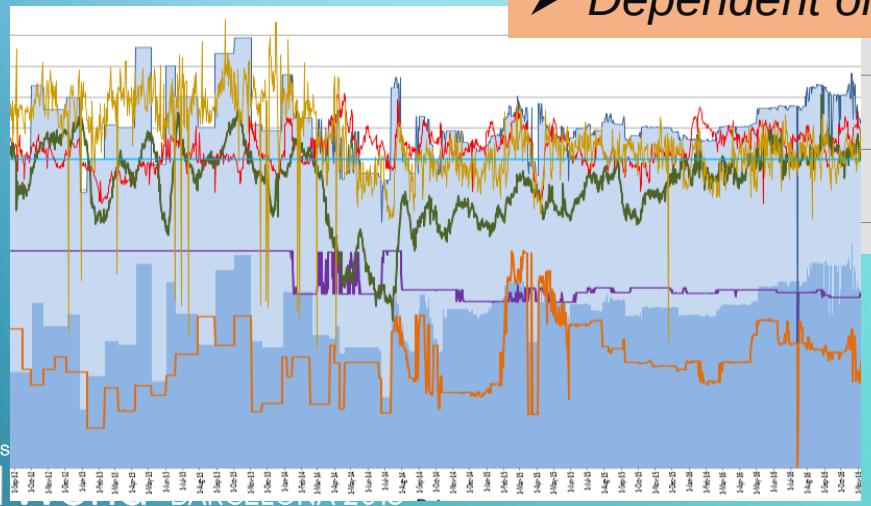
Current way of process monitoring

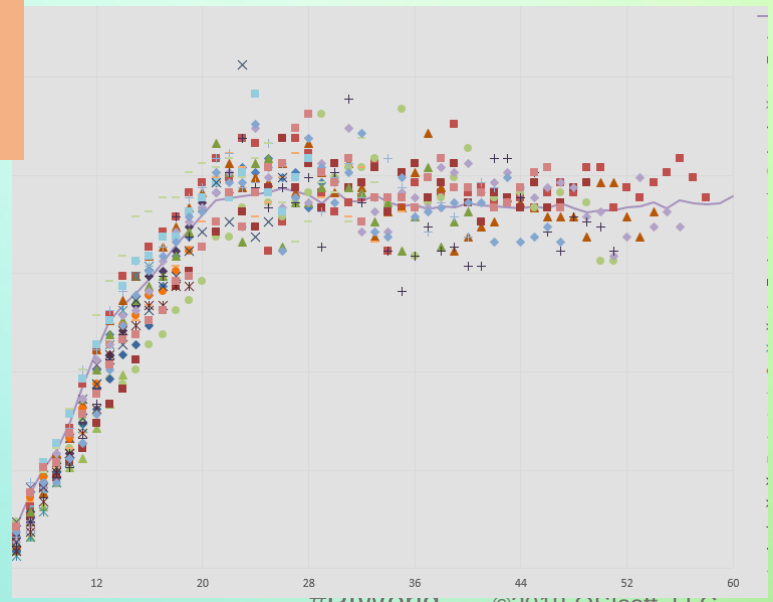






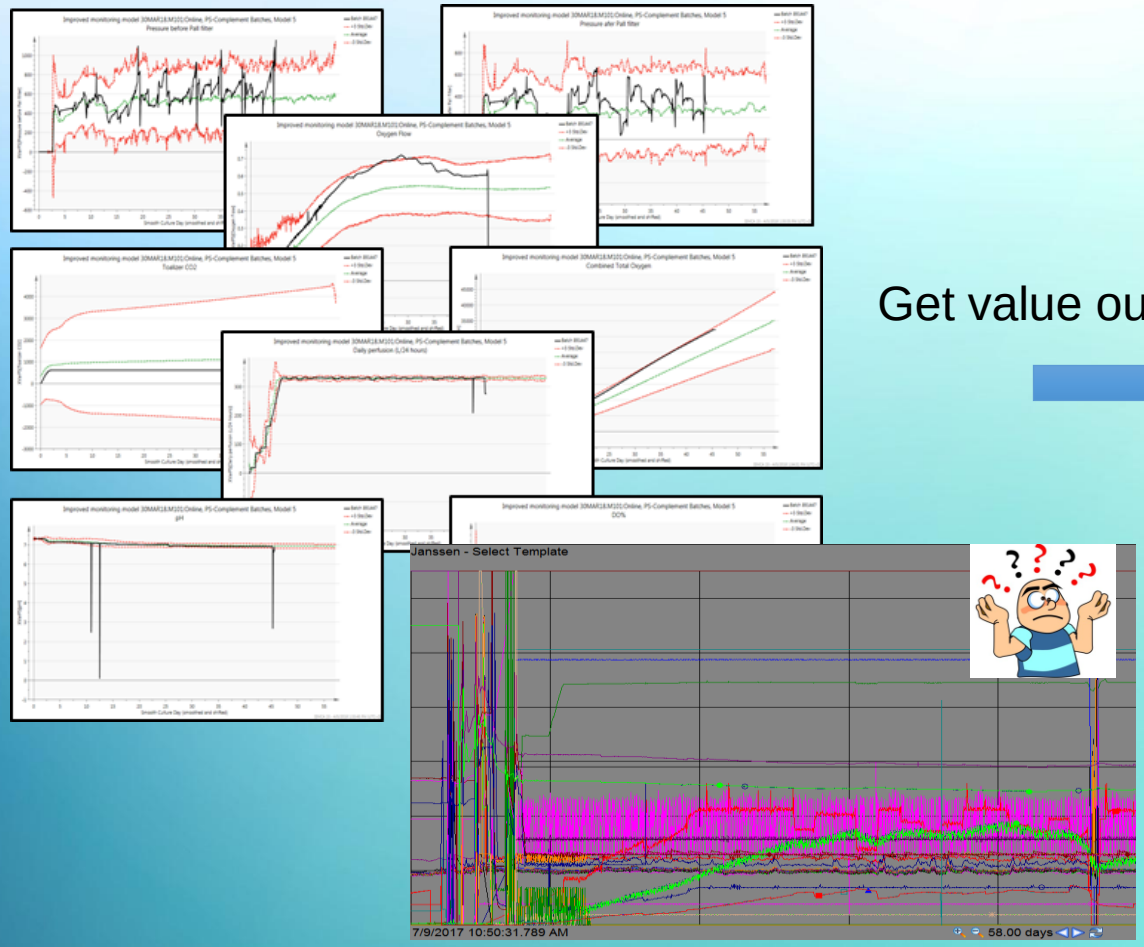
- *Useful but manually and limited!*
- *Absence of correlation between variables*
- *Dependent on experience of engineers*



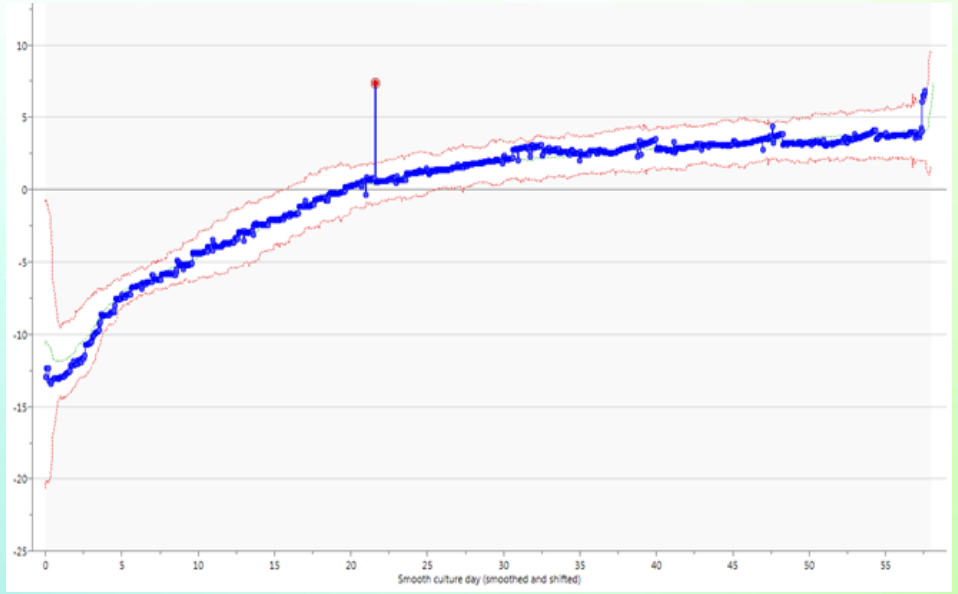


Multivariate Data Analysis

… simply means "the analysis of multiple variables at a time"

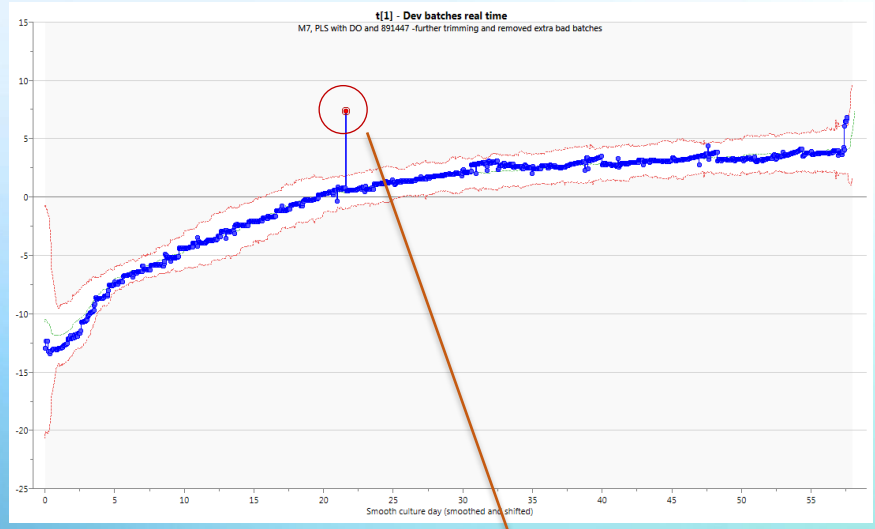


Get value out of data

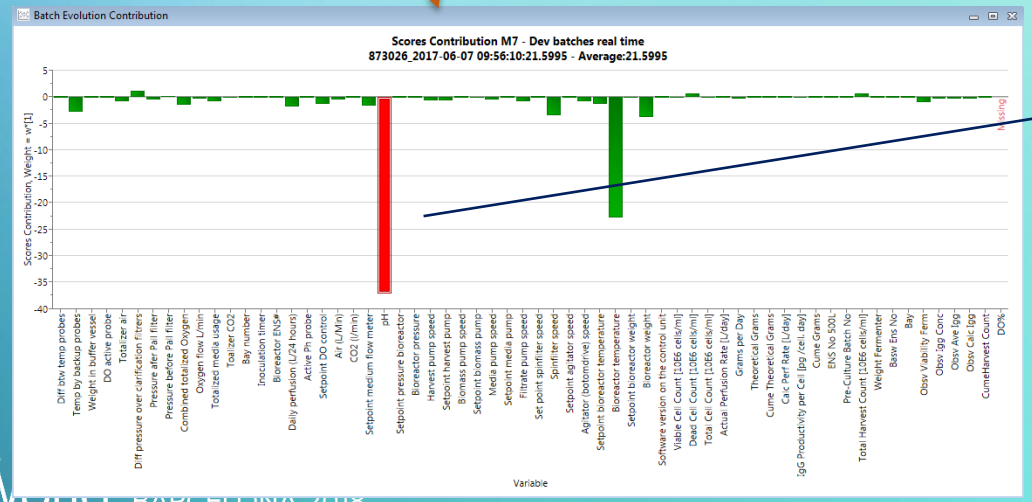


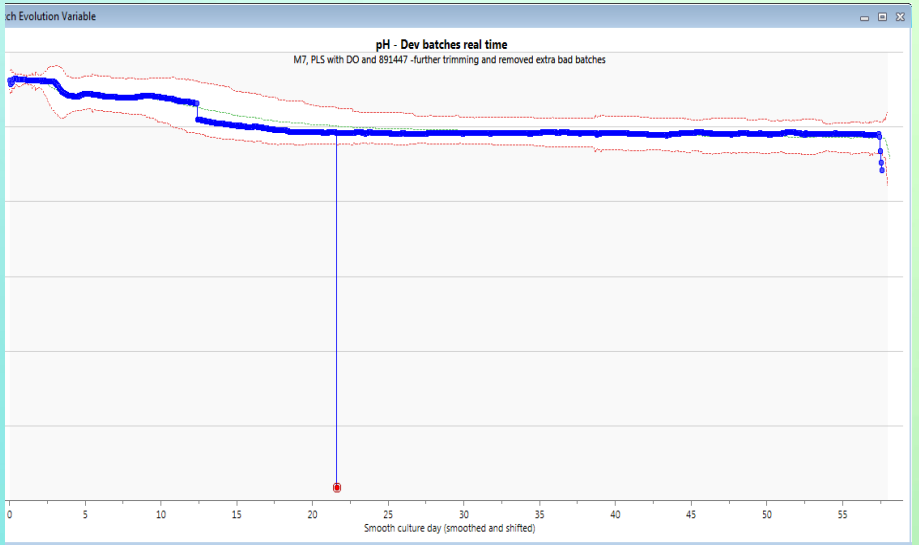
Through MVA, we can create a "summarized" parameter summarizing all variables that can be monitored in real time.

MVA with PI data and SIMCA-online:

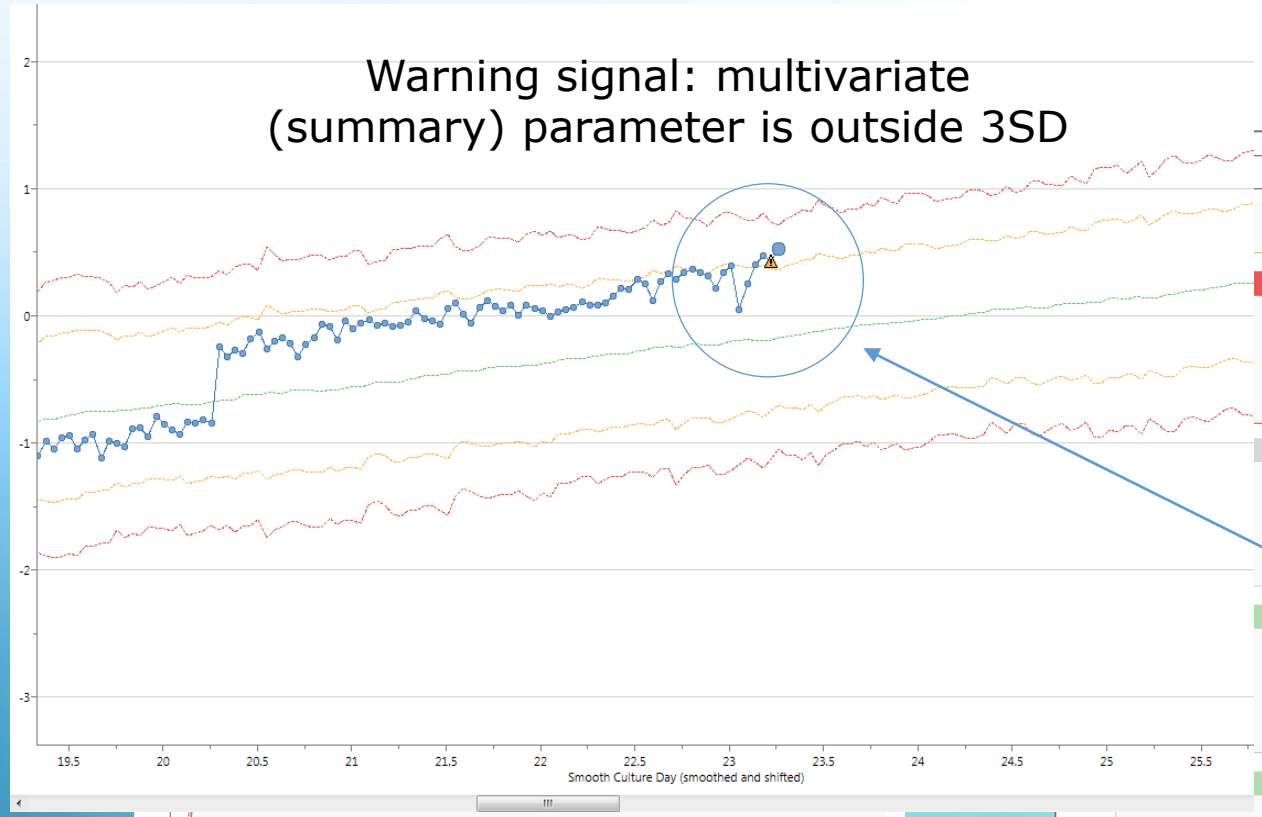


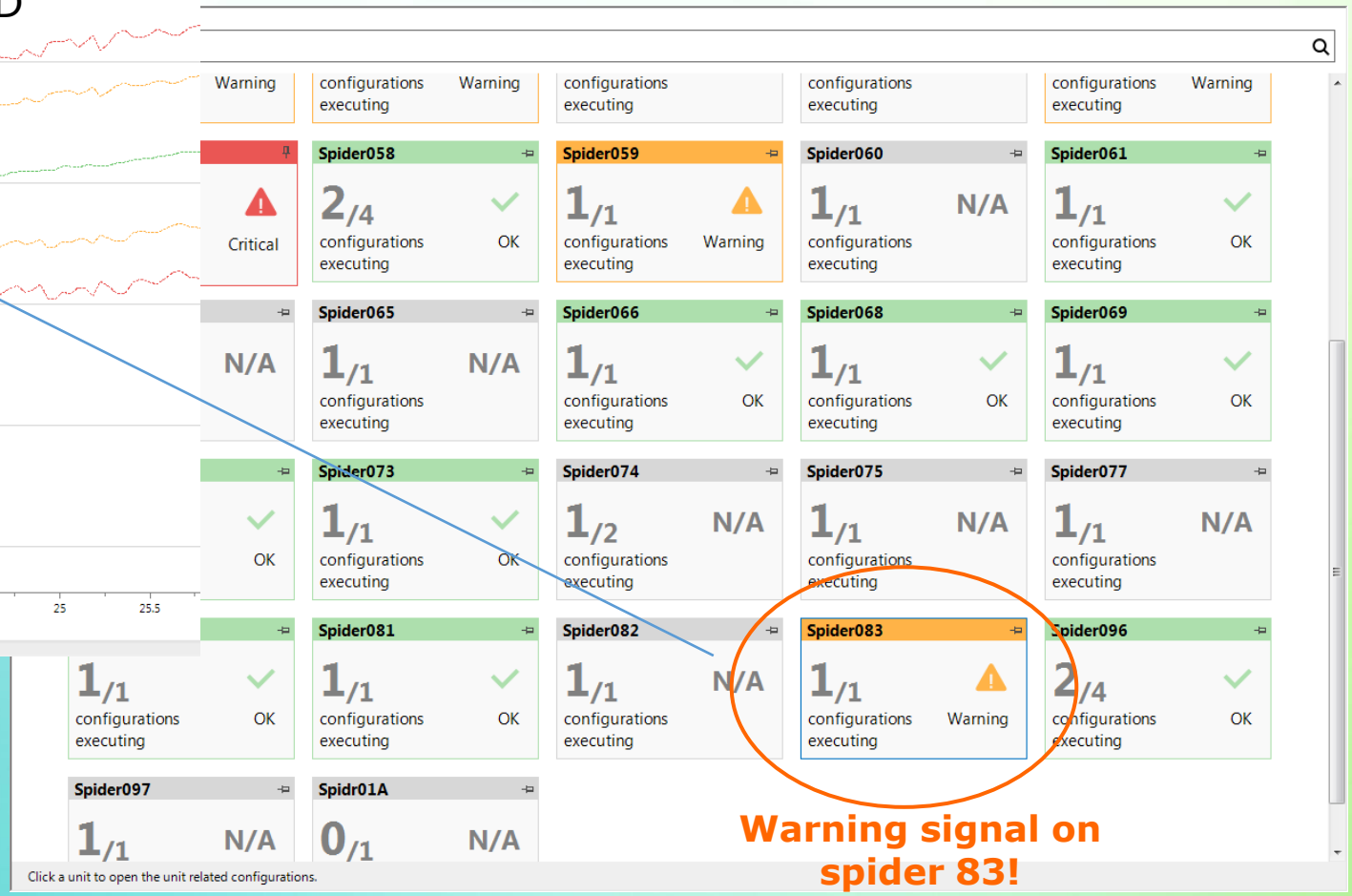
- ✓ Simple, intuitive run chart
- ✓ Easily drill down to relevant information just in a few clicks
- ✓ Overview of all variables, taking into account the correlation between them





Examples on useful MVA signals: *Online pH probe drifting*





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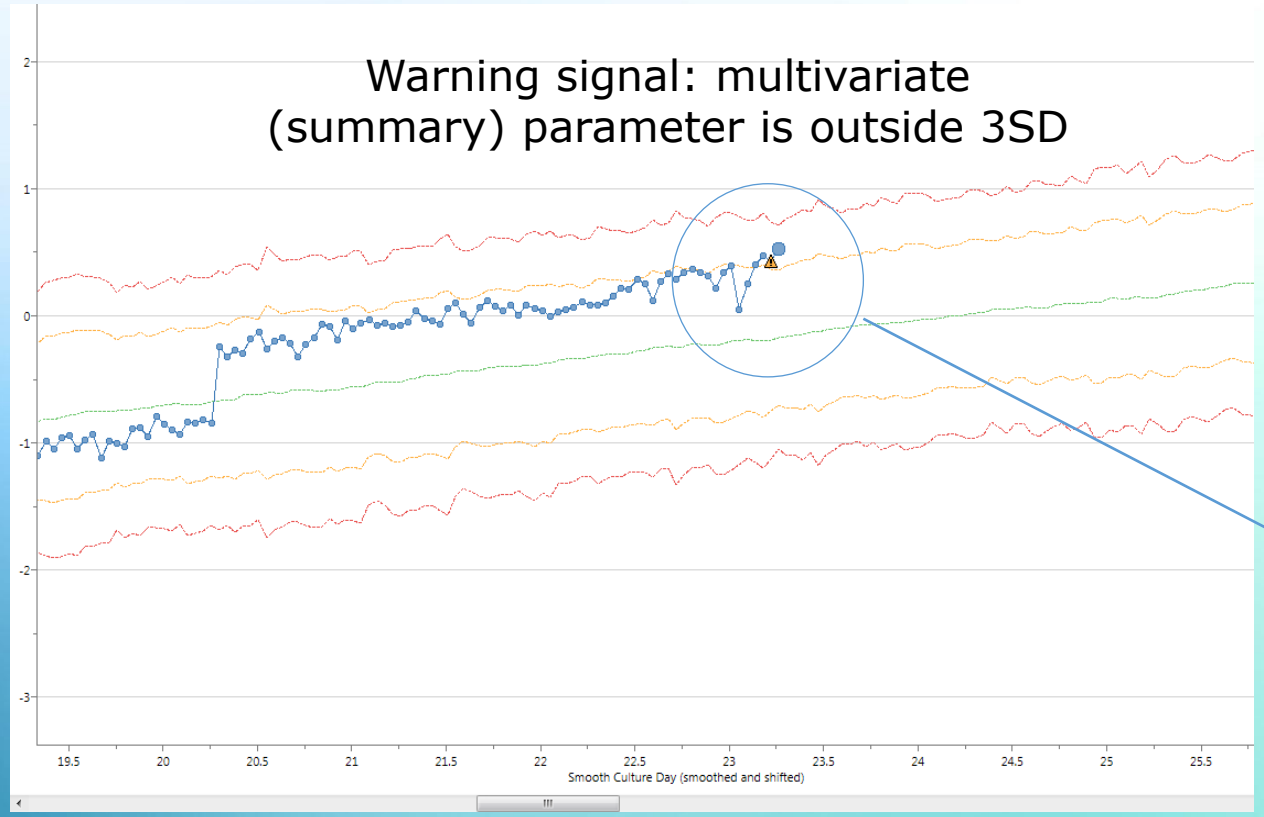
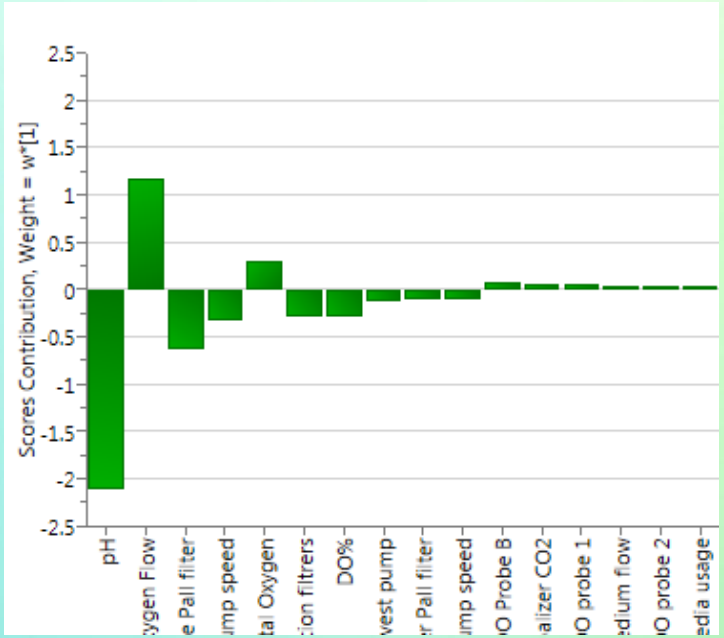


Signal related to low pH, high O2 flow…



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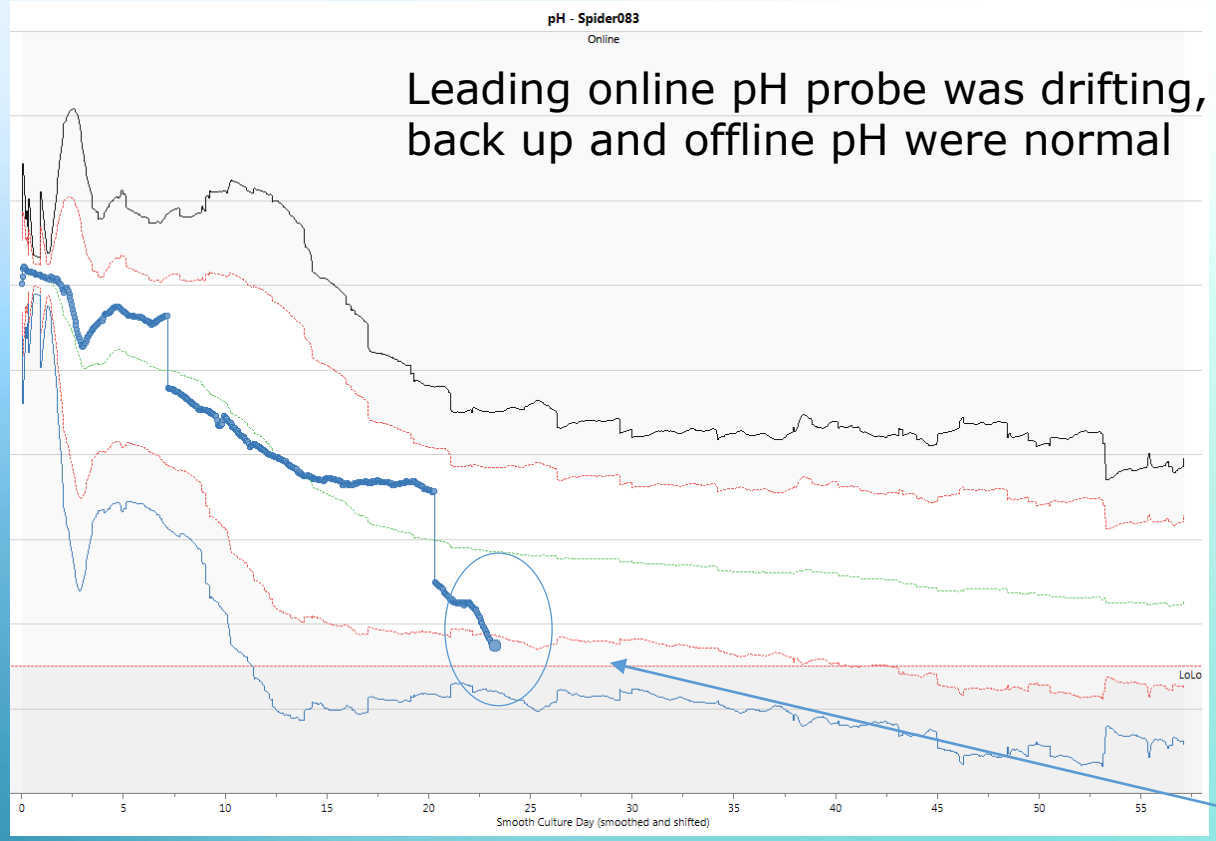

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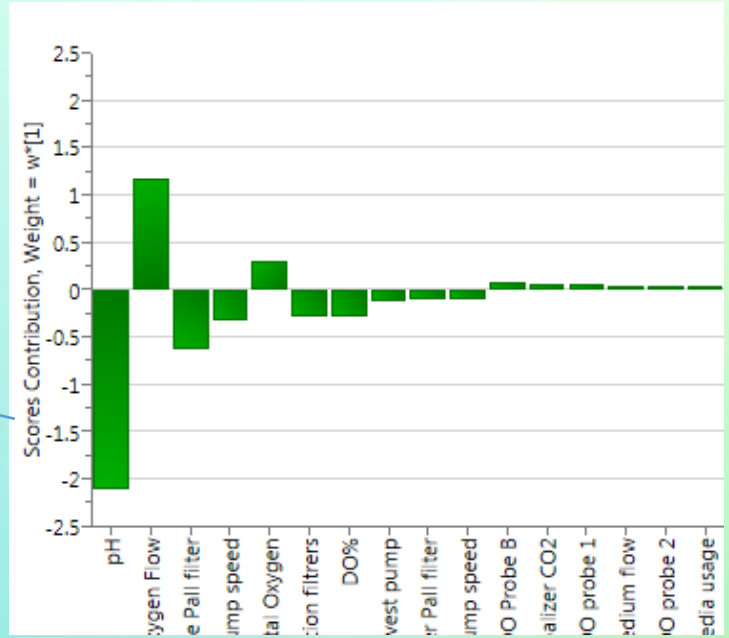

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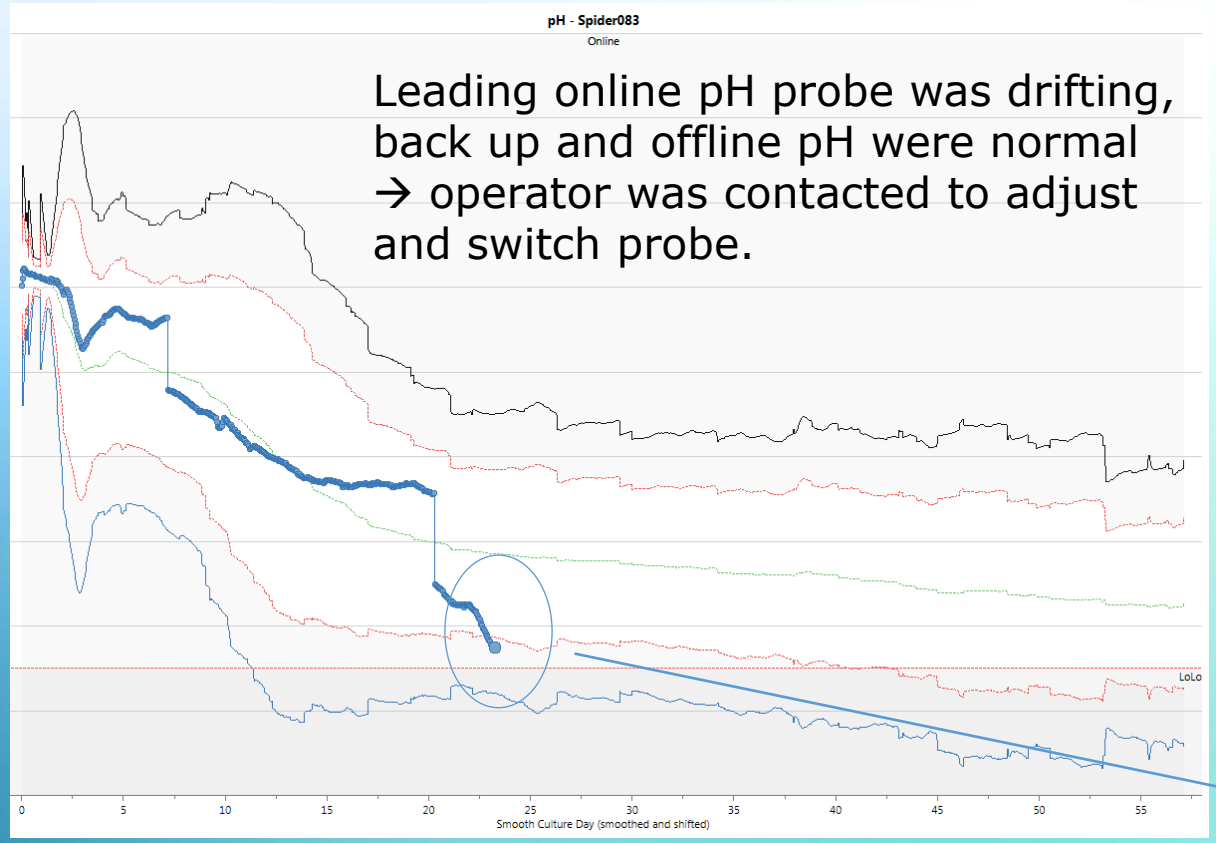
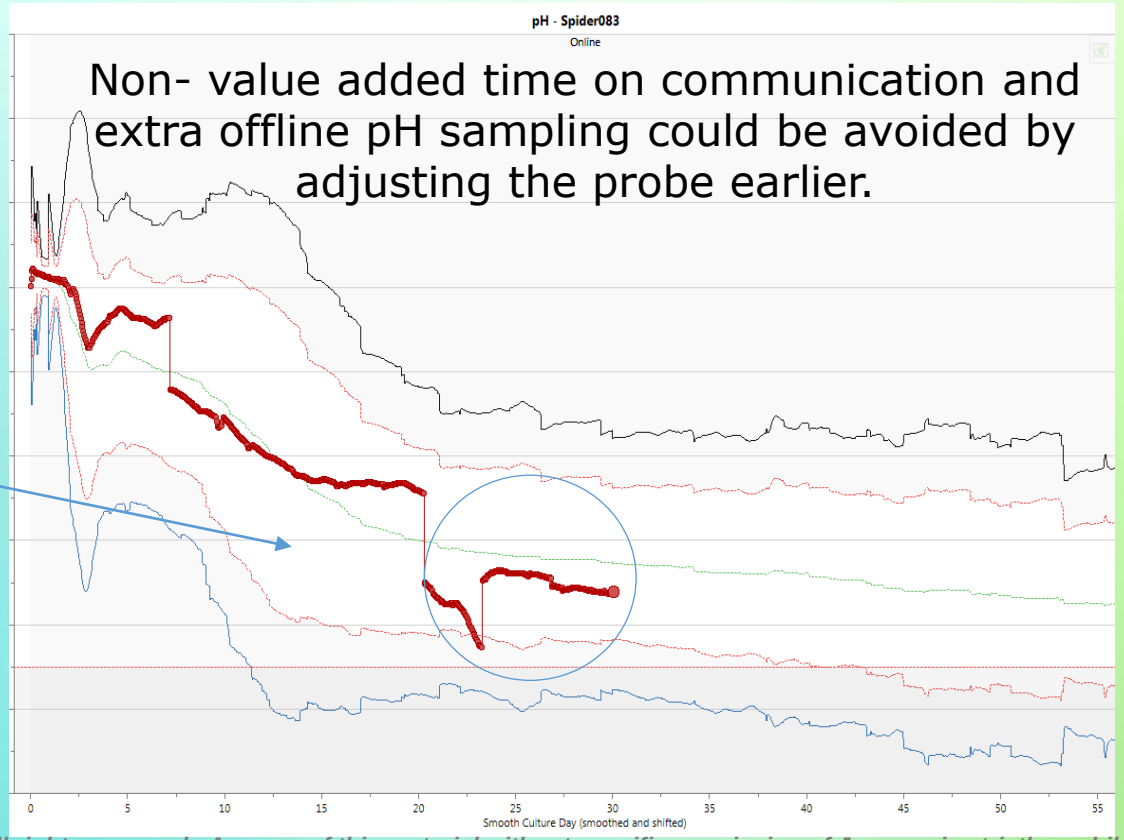
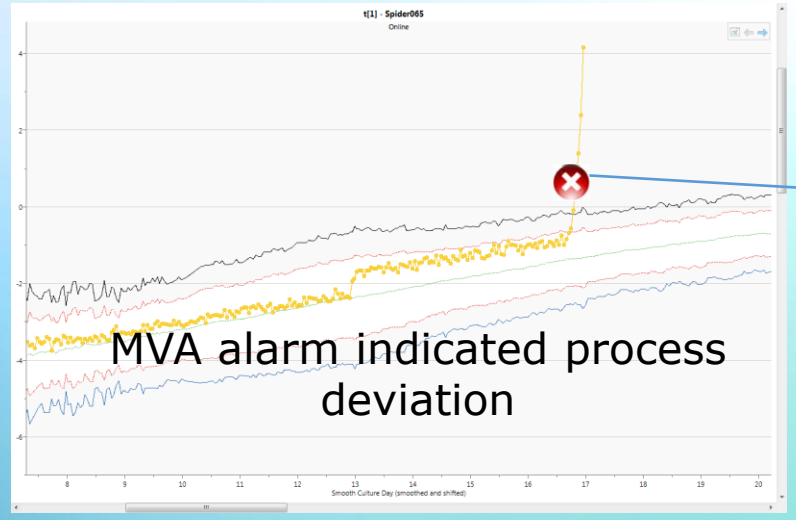
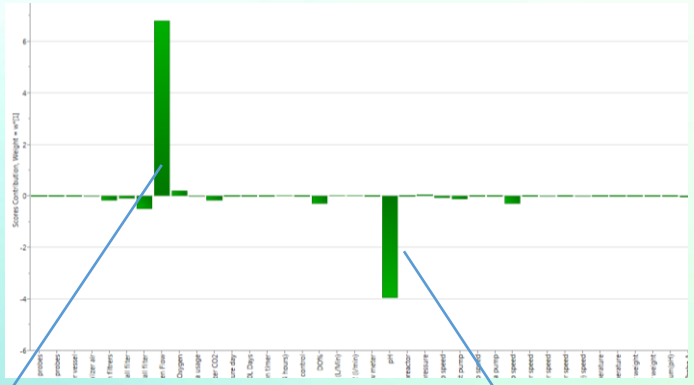


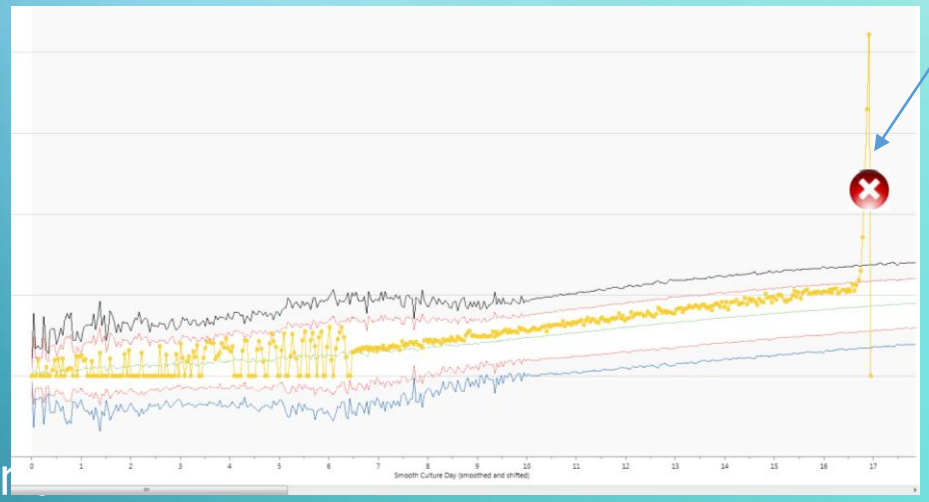


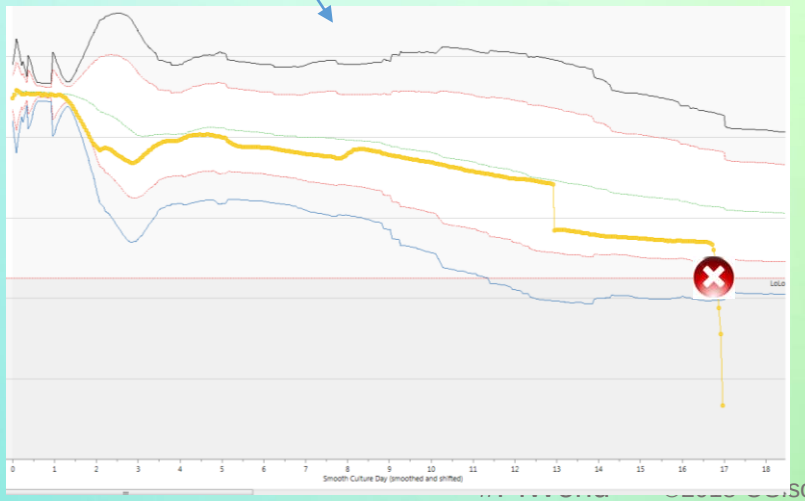
Examples on useful MVA signals: *Contamination early detection*

BRX 500L contamination: pH dropped and DO increased quickly.









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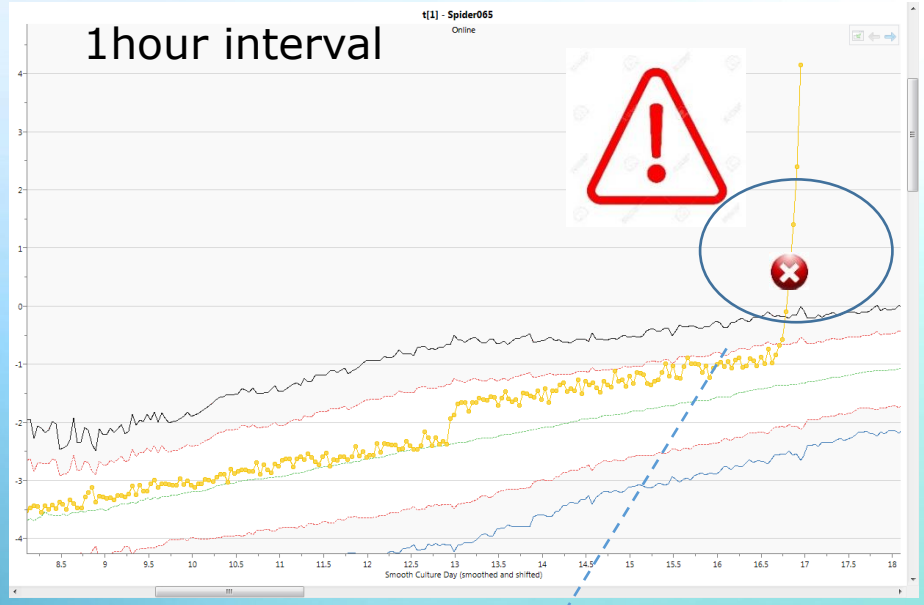
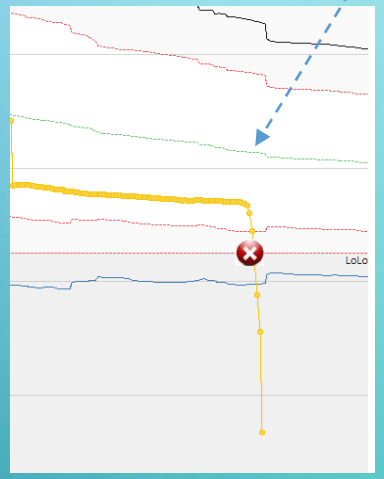
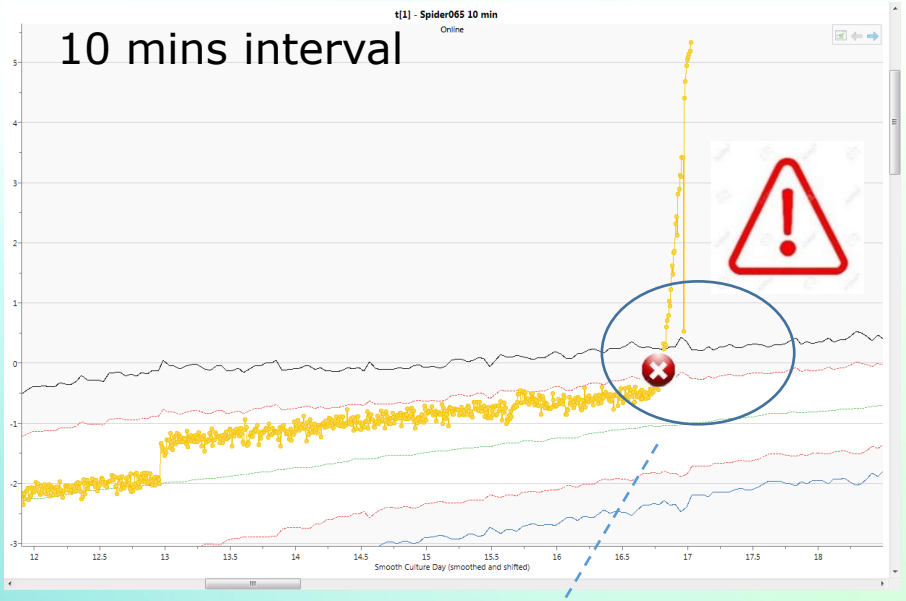
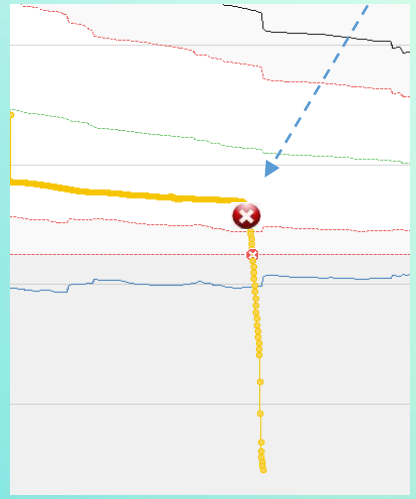




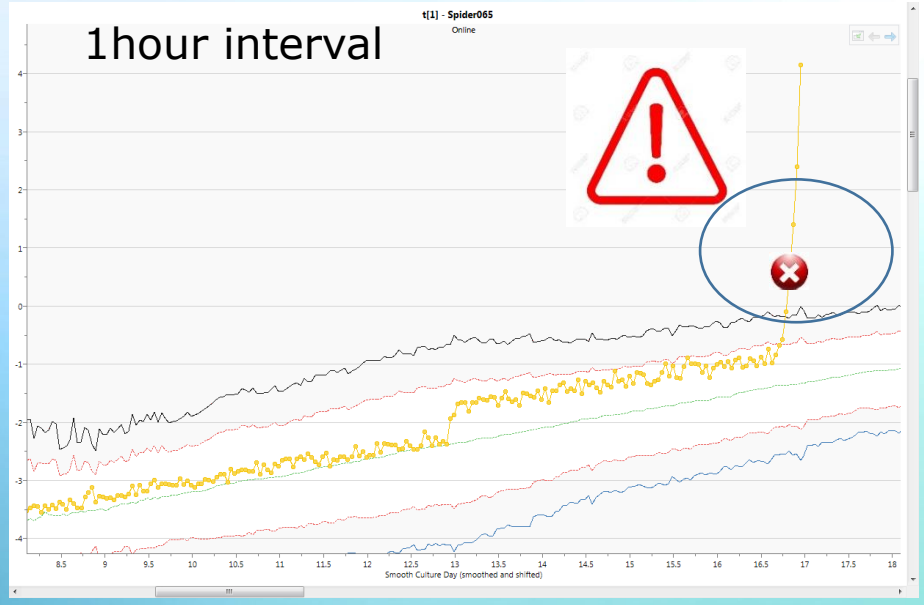
Warning at the same time of out of specification alarm

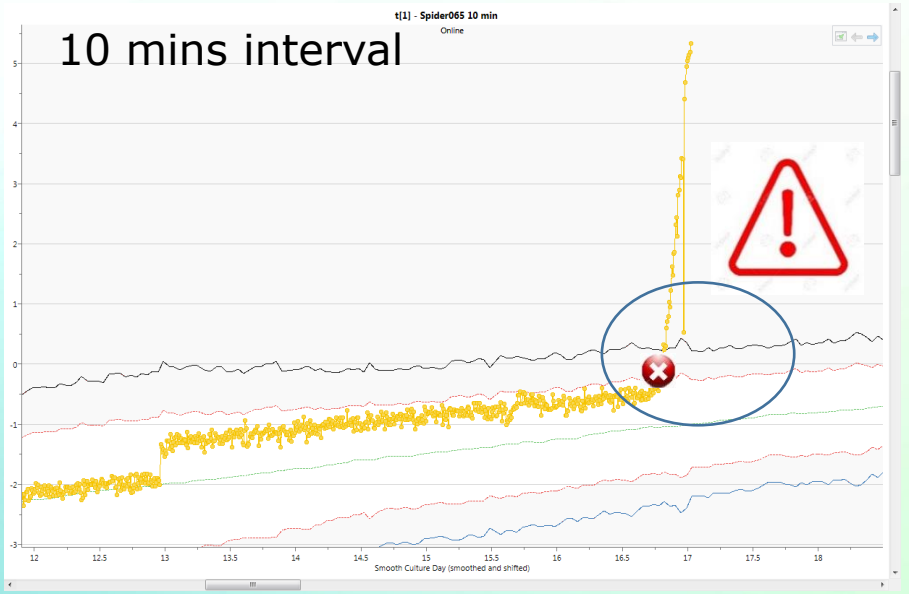




Warning 2 hrs before pH dropped to lower specification limit

Examples on useful MVA signals: *Contamination early detection*





Although the MVA (10min interval) cannot prevent the contamination, it can give early warning, which could help preventing pooling the contaminated harvests to the non-contaminated ones, leading to saving up to 1 DPC batch (~€200k).

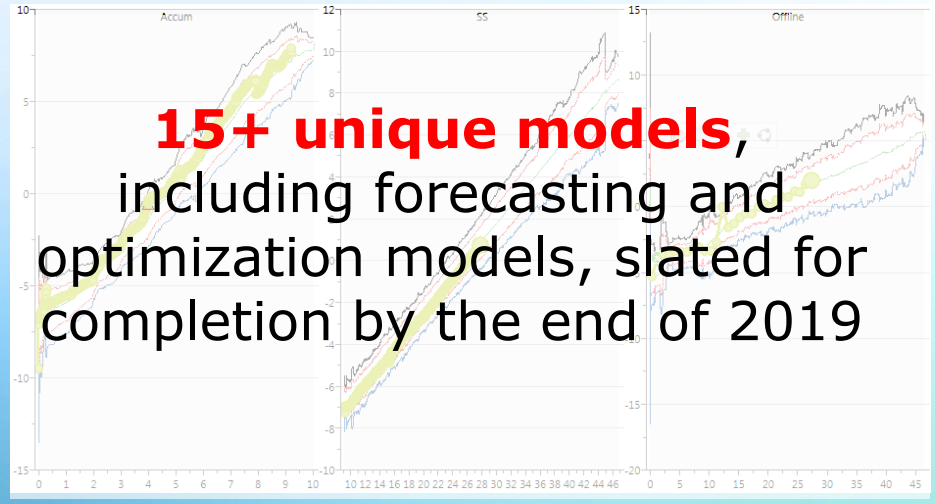
Deployment of SIMCA-online at Janssen Globally (*Prometheus*)

2017
LM Malvern Q1

2018
LM Leiden Q1
LM Cork Bio Q1
SM Cork Chem Q1

2019+
CAR-T Raritan
Solids Gurabo
Solids Latina
Solids Xi'an
SM Geel
FF Schaffhausen

Deployment of SIMCA-online at Janssen Globally

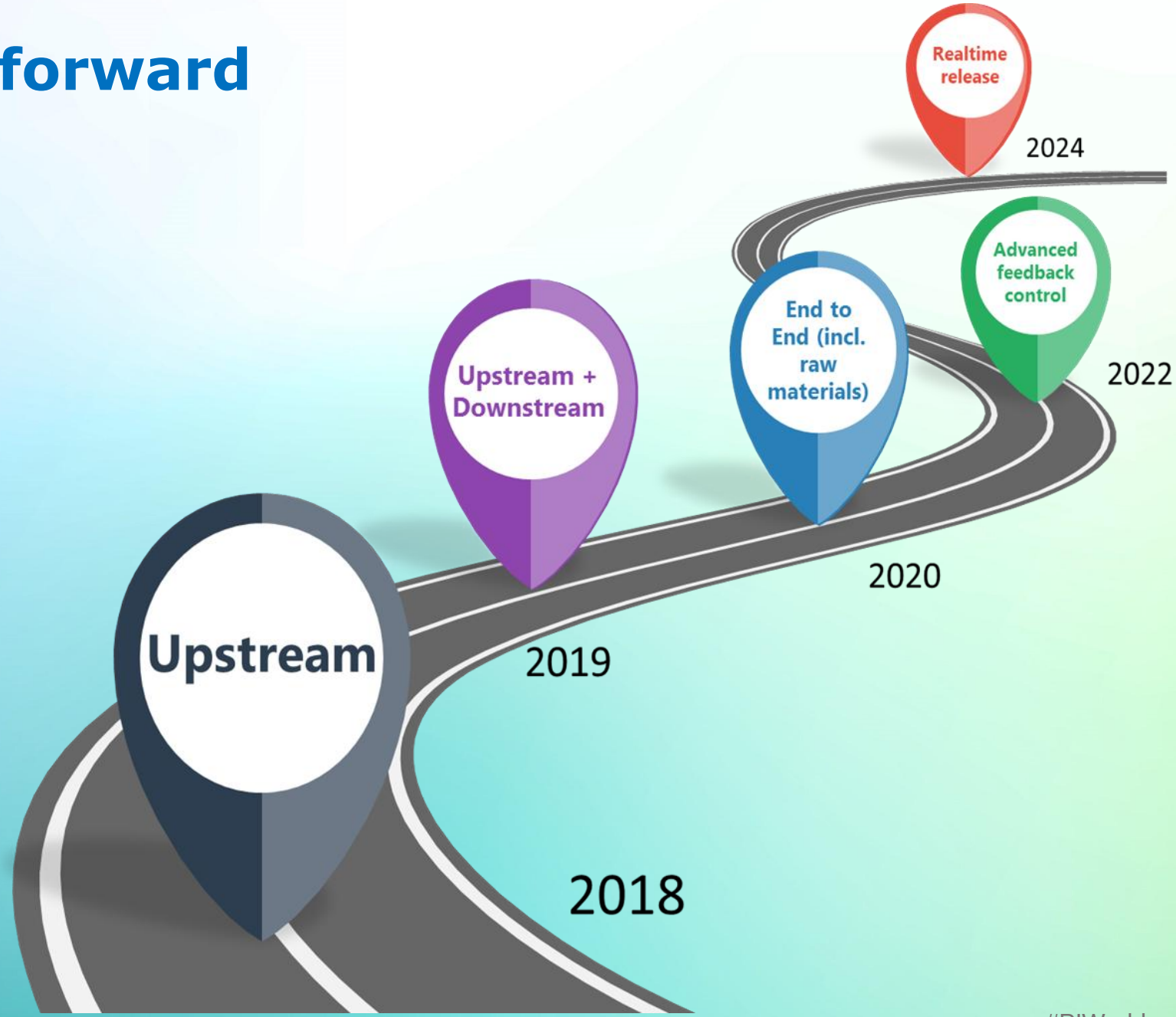


15+ unique models, including forecasting and optimization models, slated for completion by the end of 2019

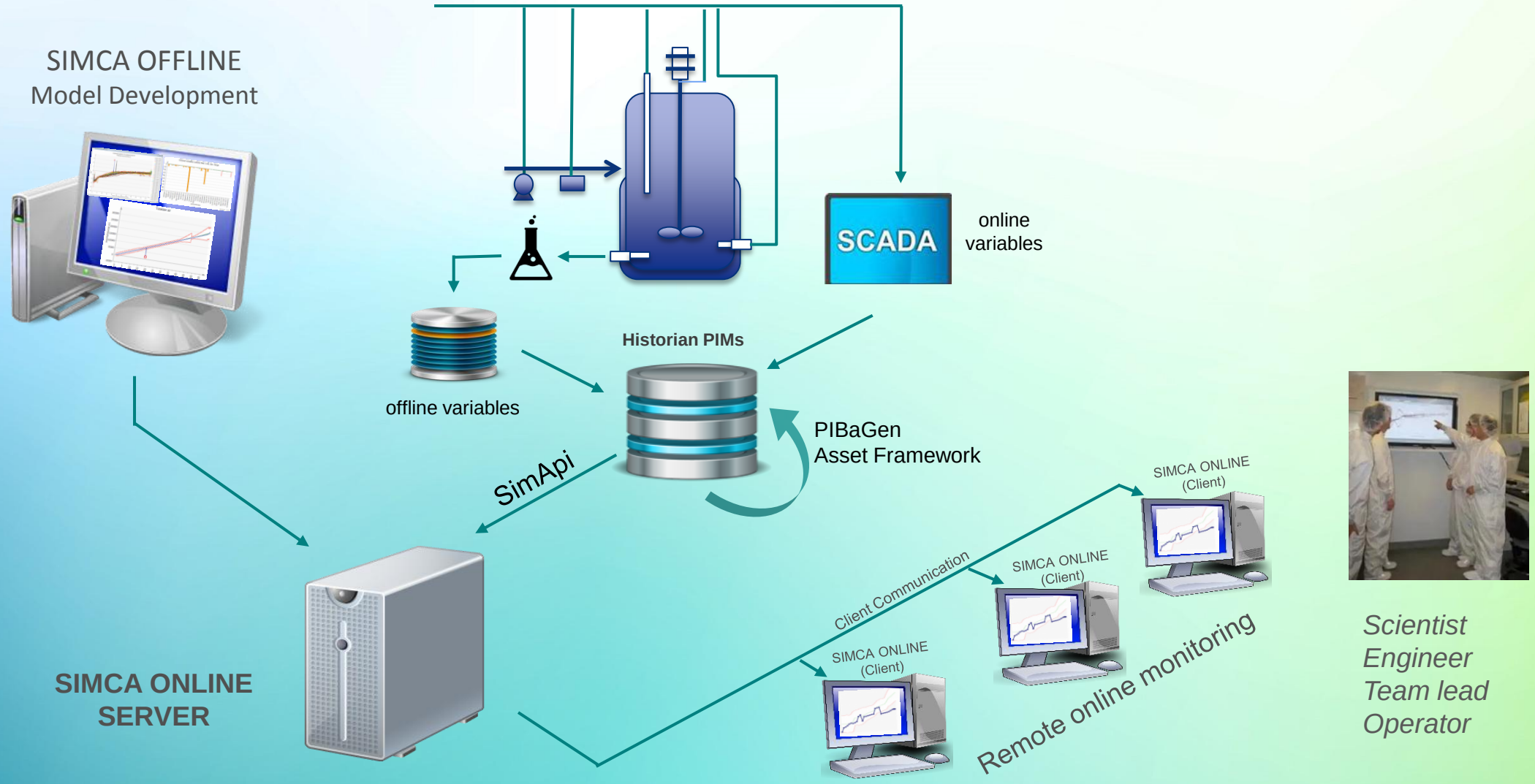
1.5 million+ saved since program started

Global training and standards created to support rapid deployment

RTMVA path forward



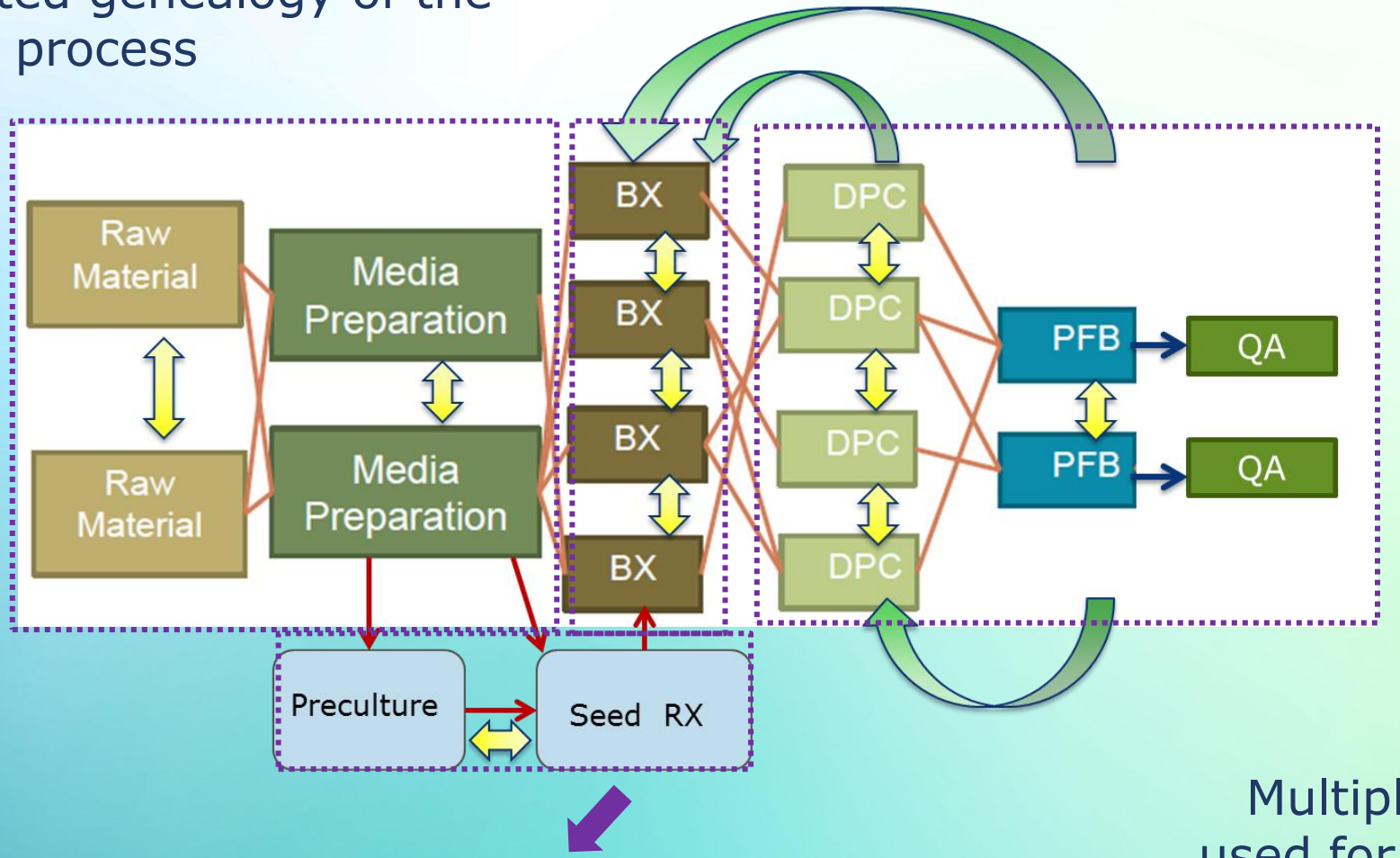
How was PI - SIMCA online server set up?



Scientist
Engineer
Team lead
Operator

Challenges

Complicated genealogy of the perfusion process



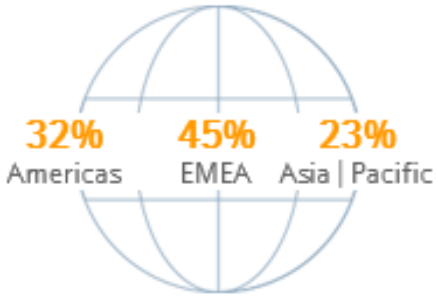
SAP
MBR/MES
Elims

SAP
Elims
MBR/MES
Local DBs

PI, MES/MBR, Local DBs

Multiple IT systems used for data storage

Sartorius at a glance



7,500
Employees

2
Divisions

CAGR
15%

Founded
1870

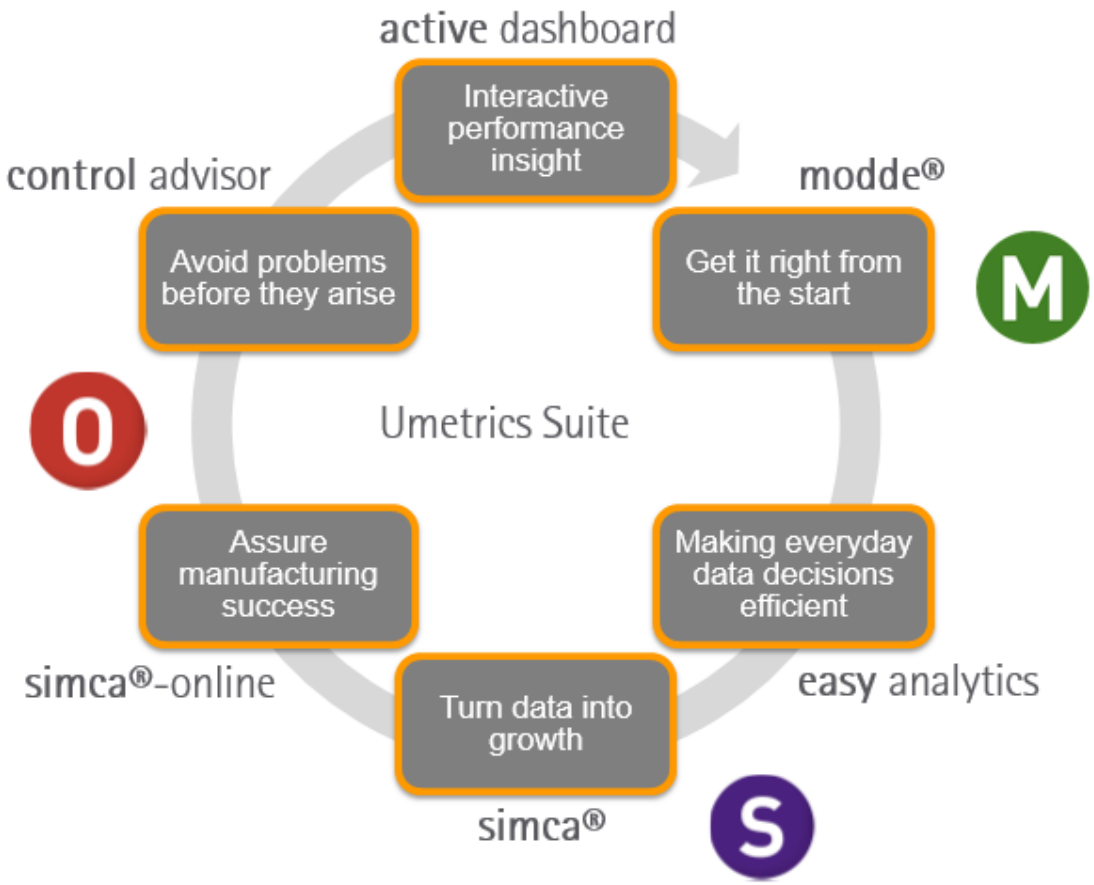
Sales
€1.4 billion

Sartorius Stedim Data Analytics

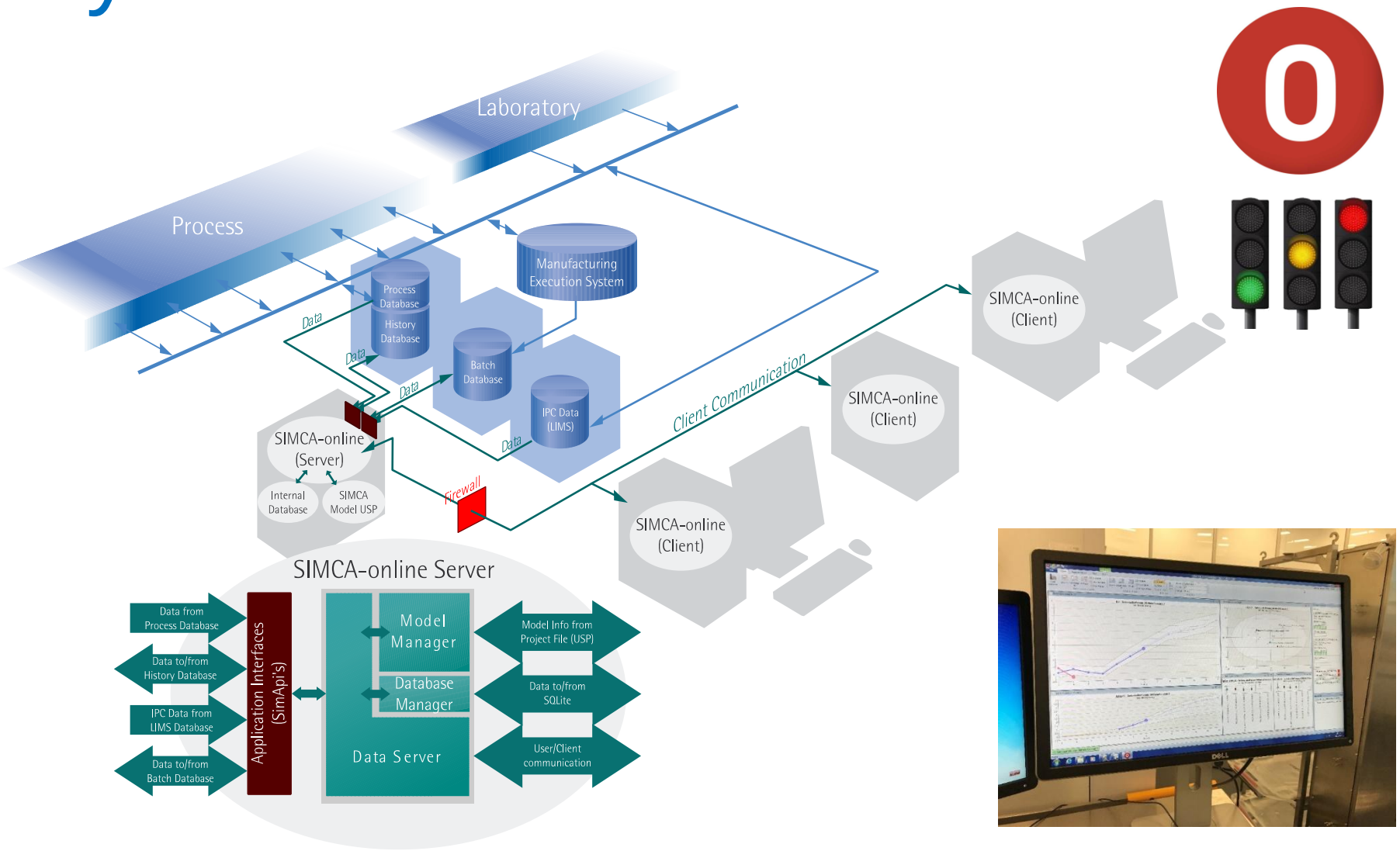
- Founded in 1987 by Professors Svante Wold and Rolf Carlson
- Acquired by Sartorius in 2017
- Product Portfolio - Umetrics™ Suite of Data Analytics Solutions
- Patented Technology

Enabling our customers to see what others don't

Umetrics™ Suite of Data Analytics Solutions

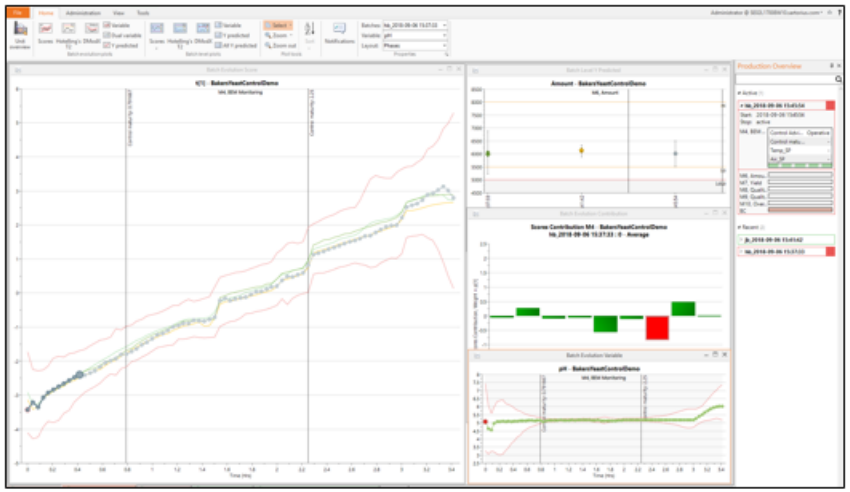


Deployment: SIMCA-online

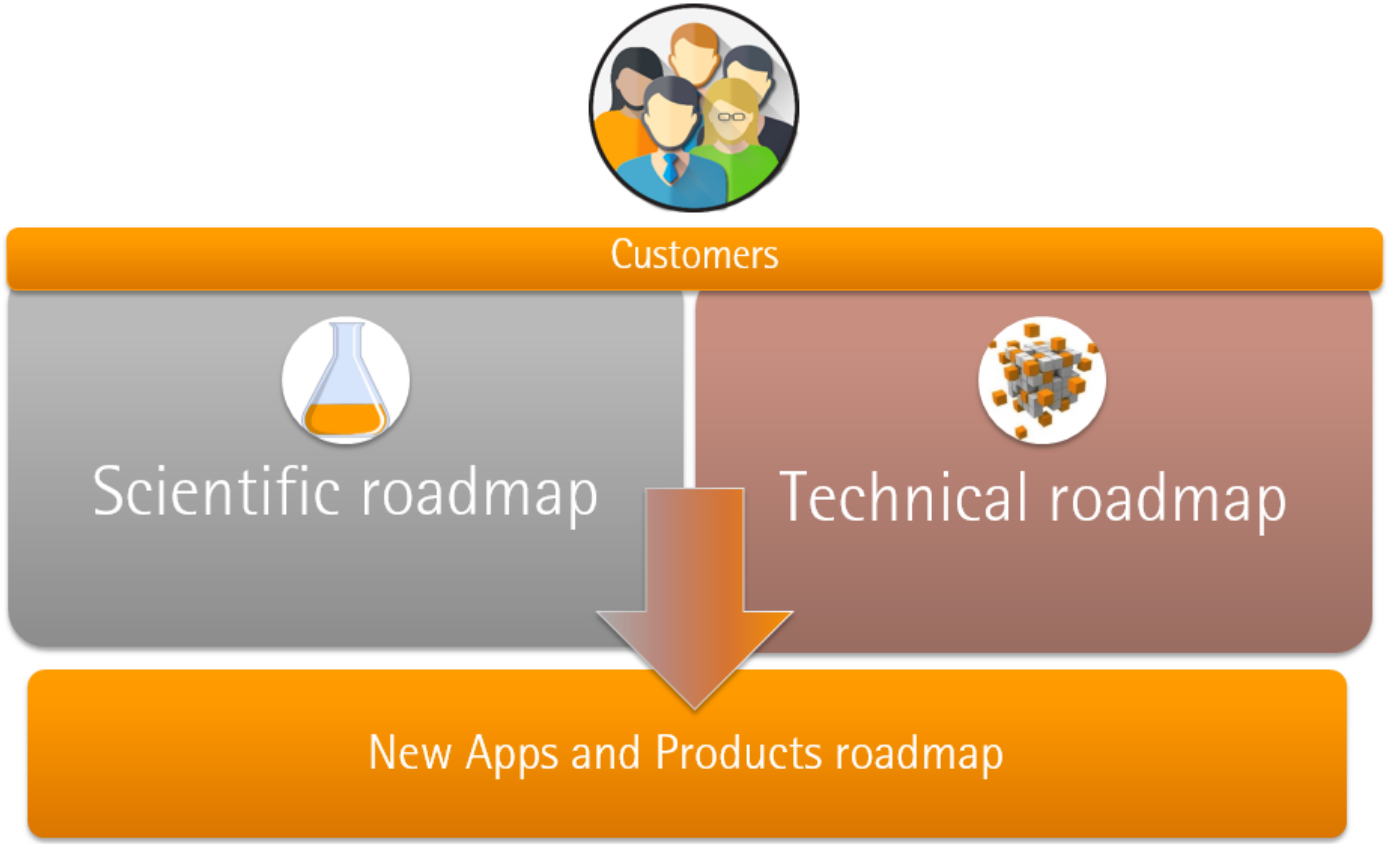


What can SIMCA®-online do on top of OSI PI AF

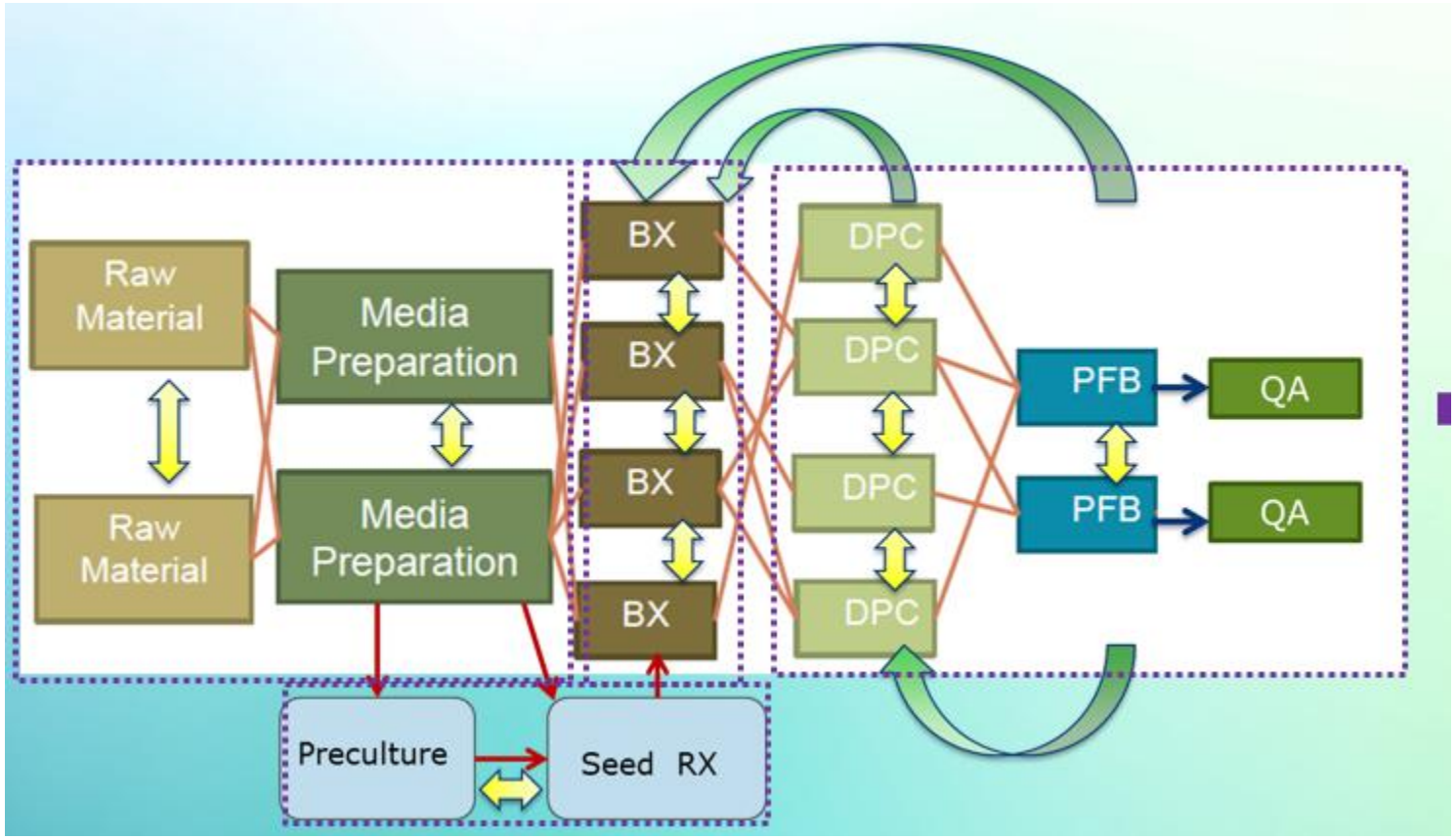
- Monitoring of "Golden batch"
- Forecasts of "what will happen"
- Stable production advisor
- Process improvements
- Soft sensor of final product quality
- Root cause investigation
- Ahead of time fault investigations



Umetrics® Suite roadmaps

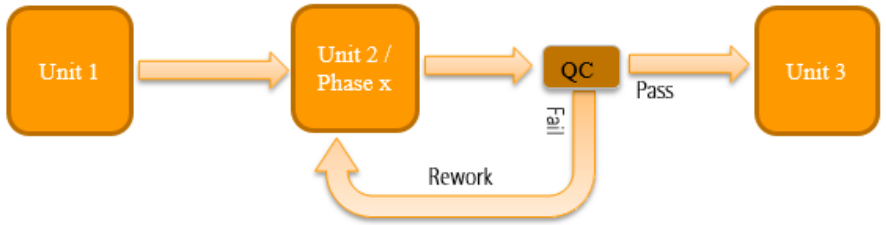


Janssen challenge

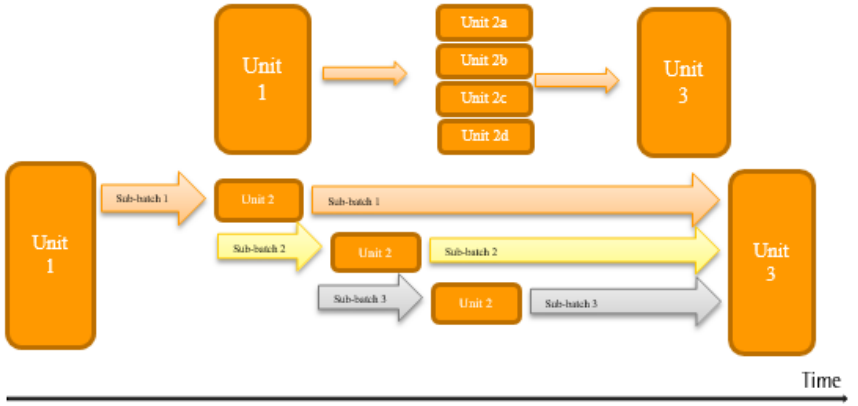


Recurrence of batches and phases

- Batch processed in same phase more than once
  - Failure to meet quality/reworks
  - Processing failure

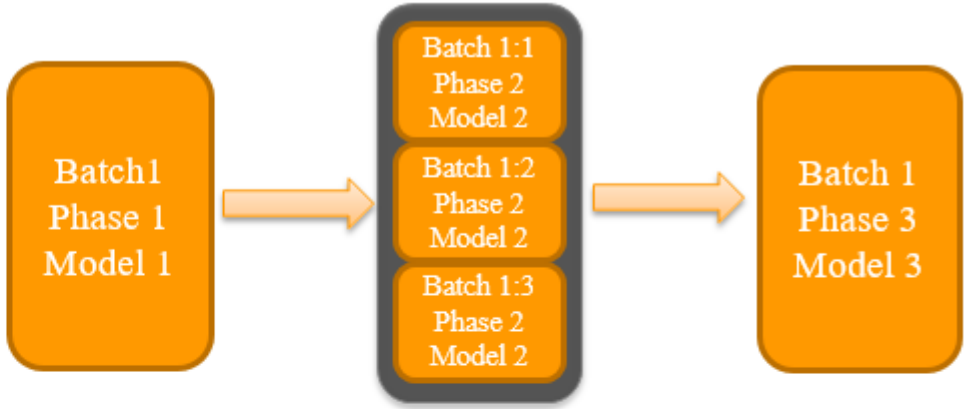


- Batch divided into separately processed sub-batches
  - Complex genealogy



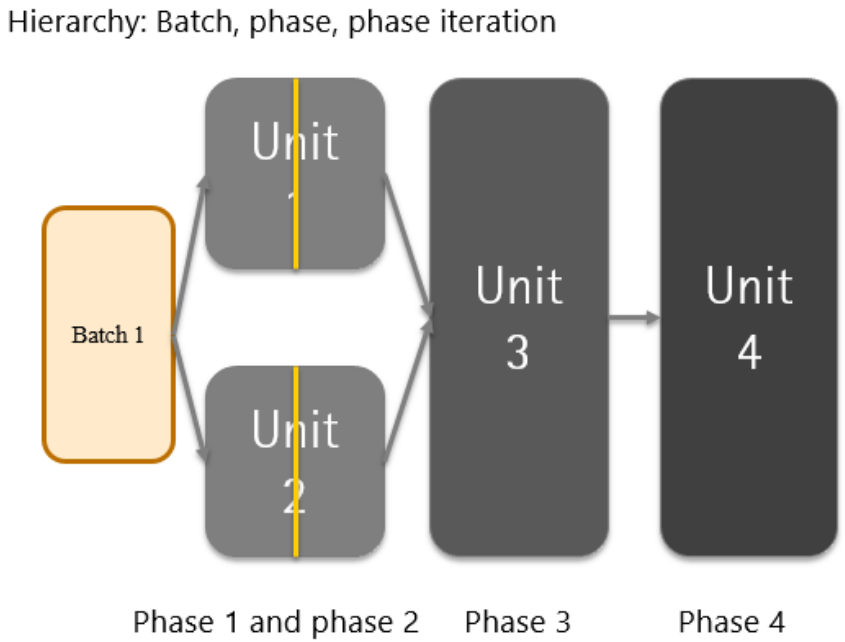
Customer challenges addressed

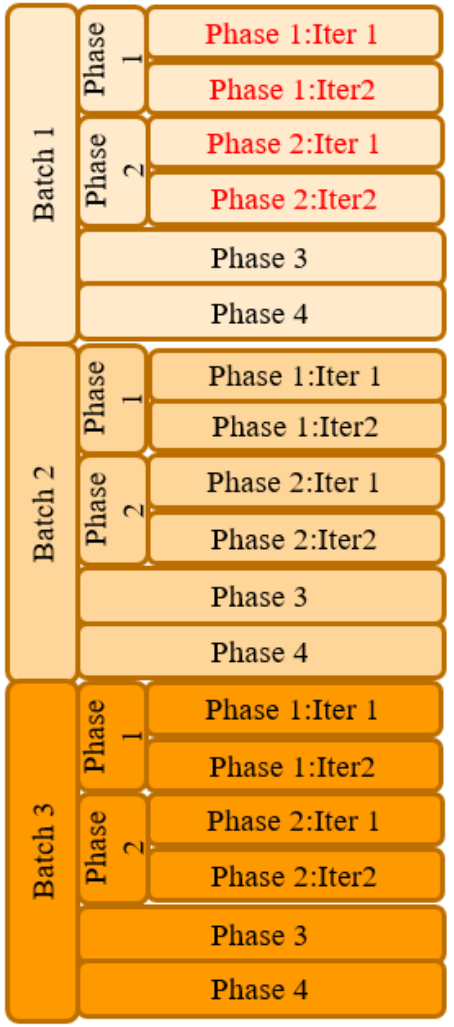
- Recurring phases in upstream and downstream processing



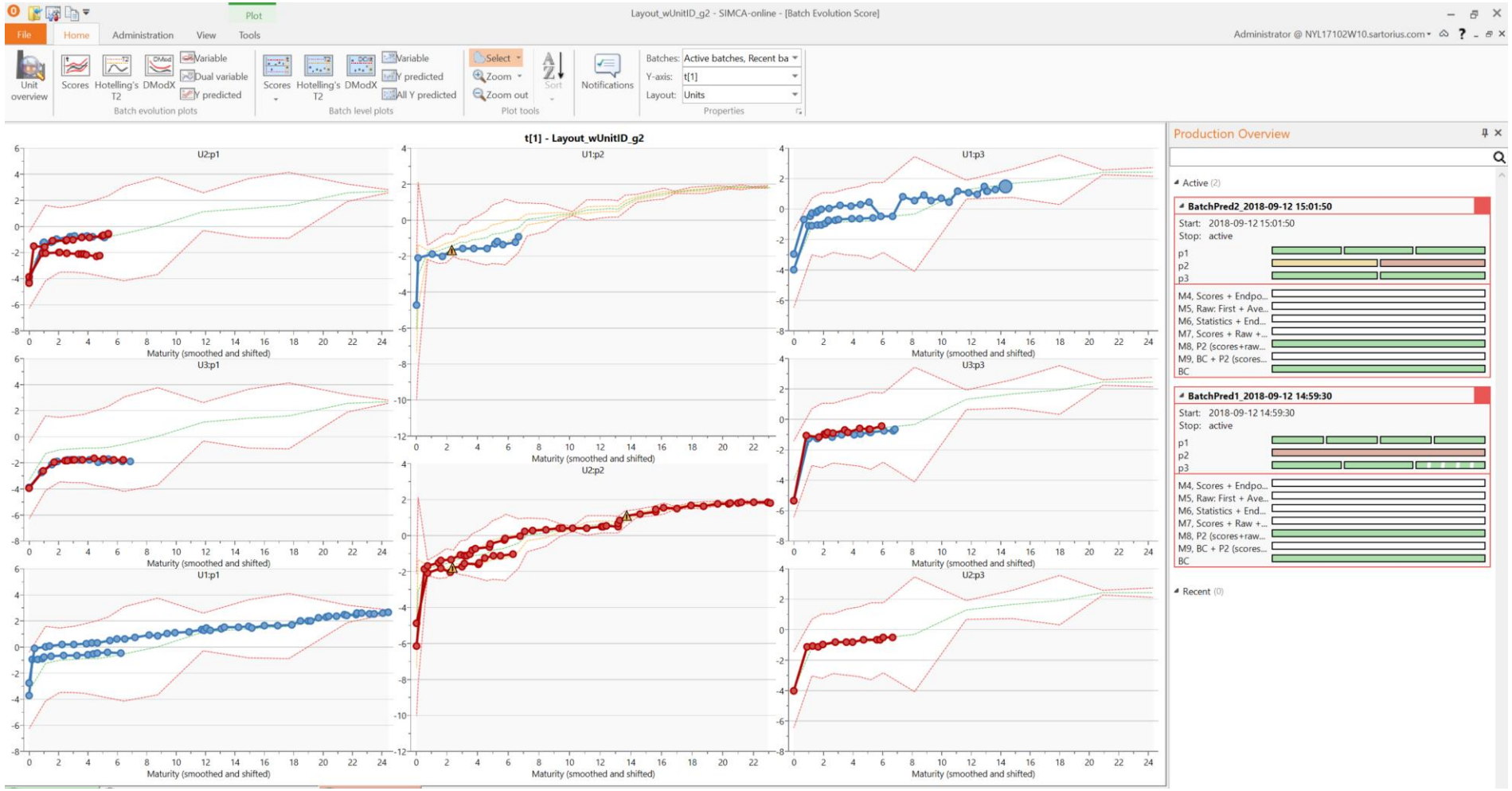
- Ability to combine all data for the batch
  - CPV
  - Quality/output prediction
  - Comparing unit performance

Data Structure requirements





Batch phase iterations in SIMCA-online



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CHALLENGE

Lack the overview of process variables, leading to undesireable number of process deviations

- pH drifting
- Bioreactor contamination

SOLUTION

Combine PI and SIMCA-online to enhance early process fault detection

- Employed at multiple sites
- Modelled by process scientists
- Utilized by engineers
- On-going pilot at manufacturing operations

RESULTS

Early warning of process excursions results in less process deviations

- RT-MVA is an intuitive monitoring tool
- >1.5 millions saved across sites since the program started

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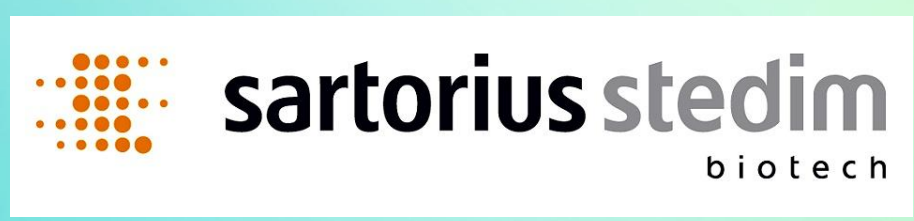
Thank you!



Back up