



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

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Anna Persson





Prometheus project

.... a journey to
Advance Process Control

Johnson & Johnson

Consumer



Medical Devices & Diagnostics



Pharmaceutical



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



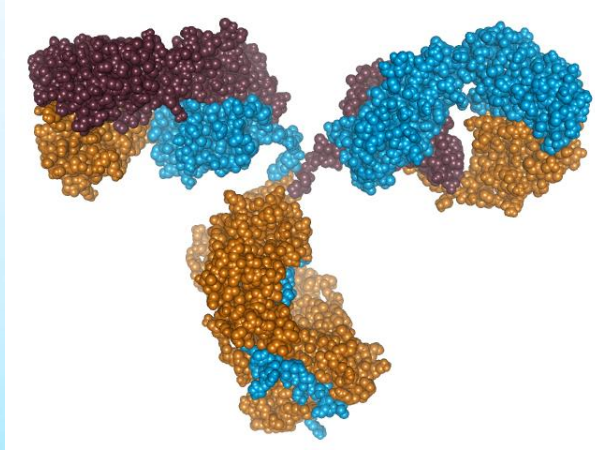
6.9

billion USD

R&D investments in 2016



Janssen Biologics – The Netherlands

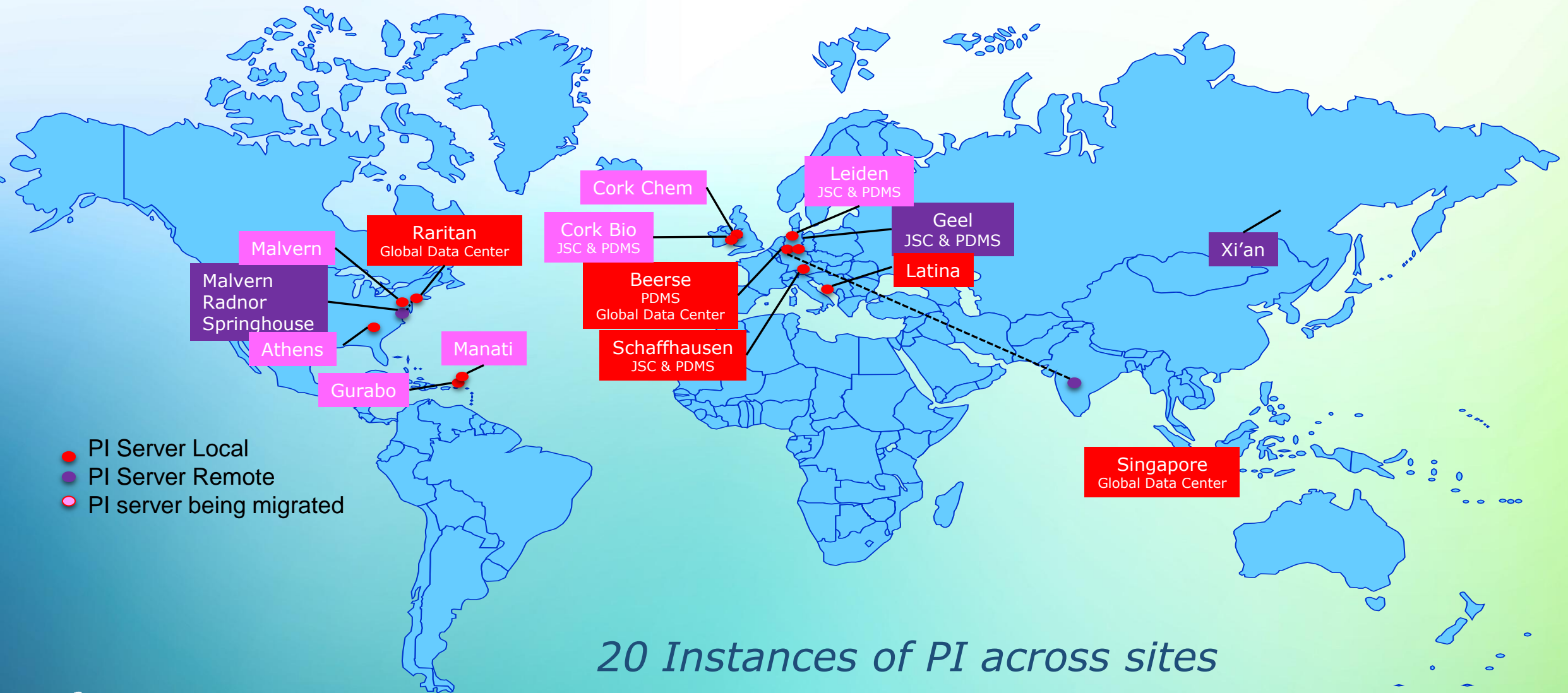


- **Cardiovascular**
- **Immunological disorder**
- **Cancer**

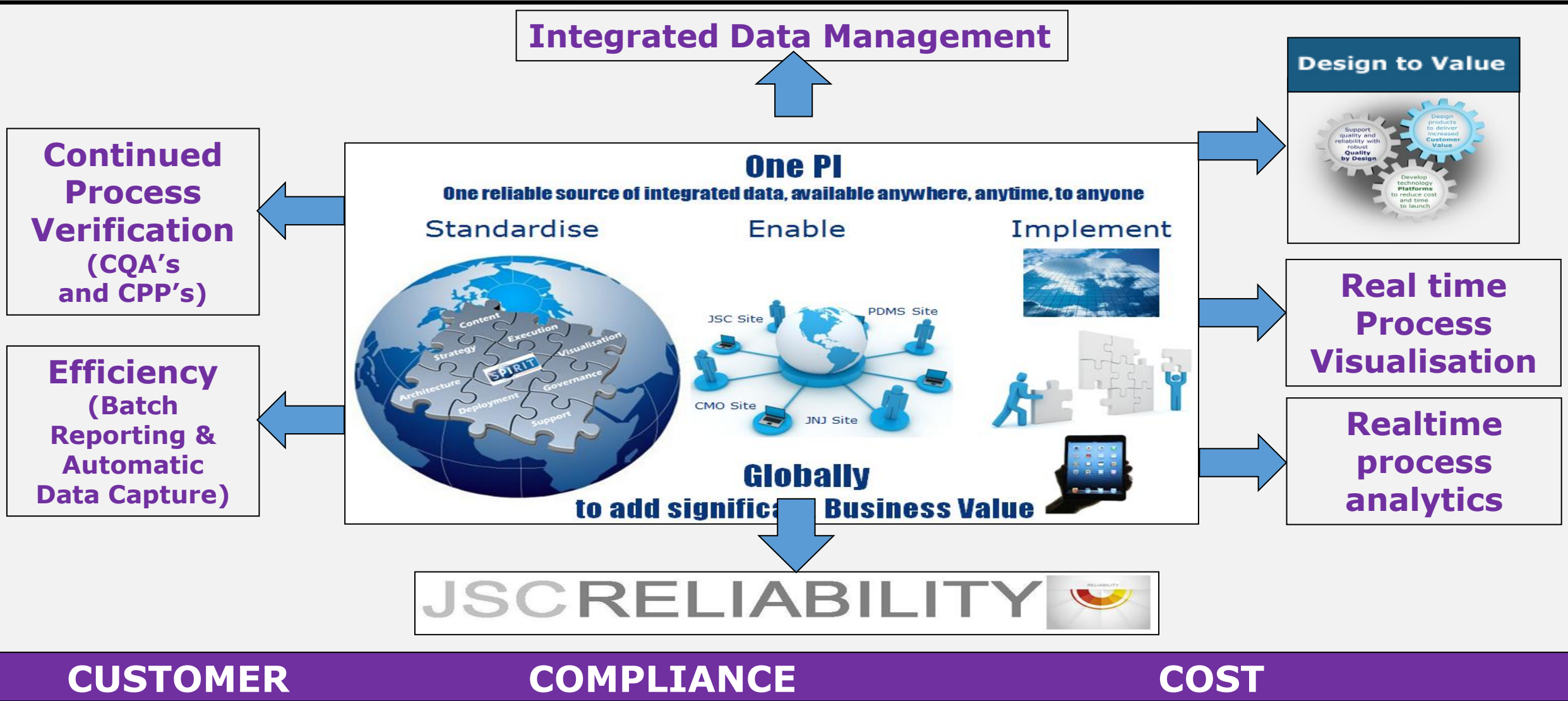
“We produce products that improve the quality of life of our patients, now and in the future”



PI system Architecture Overview



Vision: Optimizing Global Deployment of PI system



Business Challenges

I need to approve and release these batches faster and more efficiently

QA Representative

Business Support

I need to analyze all this process data for cycle time and performance. Where do I start?

I need visibility on all my processes in real time and I need it centrally at my desk!

Plant Manager

Maintenance Technician

I need visibility on energy usage! 150 Electrical meters, that a lot of data gathering!

Business Challenges

AAI, ABB, ACS, ADACS, Advanform, AECL, AIM, Alerton, Alfa, Allen, Alstom, Amersham, Ametek, Andover, AnnotationArray, Apron, APT, Arbiter, Areva, ARGA, ARL, ArrayData, AspenTech, Automated, AutoMax, Automess, BACnet, Bailey, Barber, Basler, Batch, Baytek, Beckman, Beckwith, Bently, BitMask, Bitronics, Bliss, Bristol, Bruker, Campbell, CANbus, Carrier, Caterpillar, Chessel, Chessell, Cincinnati, CircularBuffer, Cisco, Citicor, Cognex, Columbia, Contec, ControlLogix, Control, Cooper, CSI, Cybectec, Data, DaVinci, Davis, dBase, DDE, Delta, Digital, DLSP, DMC, DMC5, DNP, DS, Dukane, Dynamic, Echelon, ECHO, Electro, Elutics, Emerson, Energylinc, EPIC, ERFDADS, ESC8816, ESCA, Eurotherm, Event, Field, Fisher-Porter, Fish, Forney, Forry, Forte, Foxboro, Freelance, Fuji, GE, GE/Harris, GE/M, GSE, Harmony, HART, Hartmann, Hathaway, Hitachi, Honeywell, ICCP, IEC, IFS, Impact, Inductive, InStep, Intellution, Inverse, Irajani, Kaye, L, LabVantage, LabWare, Leeds, MAX, Maxim, Metso, Micro, Microsoft, Micro, Modicon, Moore, Motherwell, Motorola, National, NDC, Neles, Nexus, O22, Oregon, ORSI, PacketCapture, Parr, Perkin, Philips, PI, Ping, Power, Queue, Quindar, Real, Relational, Reliance, Reliatronics, Rockwell, Rosemount, Schlumberger/SEME, Schneider, Sciencetech, SecondWind, SEL, Sequencia, Serck, Shell, Siemens, SIMRAD/Albatross, SISCO, SNC-Lavalin, SNMP, SOCCS, SOLAR, Spectrum, SQ-D/Telemecanique, Suzlon, Syslog, Taylor, TCP, Teledyne, Telegyr, Telog, Telvent, The, TrampClamping, Toshiba, Trane, Triconex, Universal, VAREC, Vestas, VG-Instruments, VIM, Ironix, Weschler, Westinghouse, Westronic, WinLinx, WMI, Wonderware, Woodward, XML, Yokogawa...

Business Support

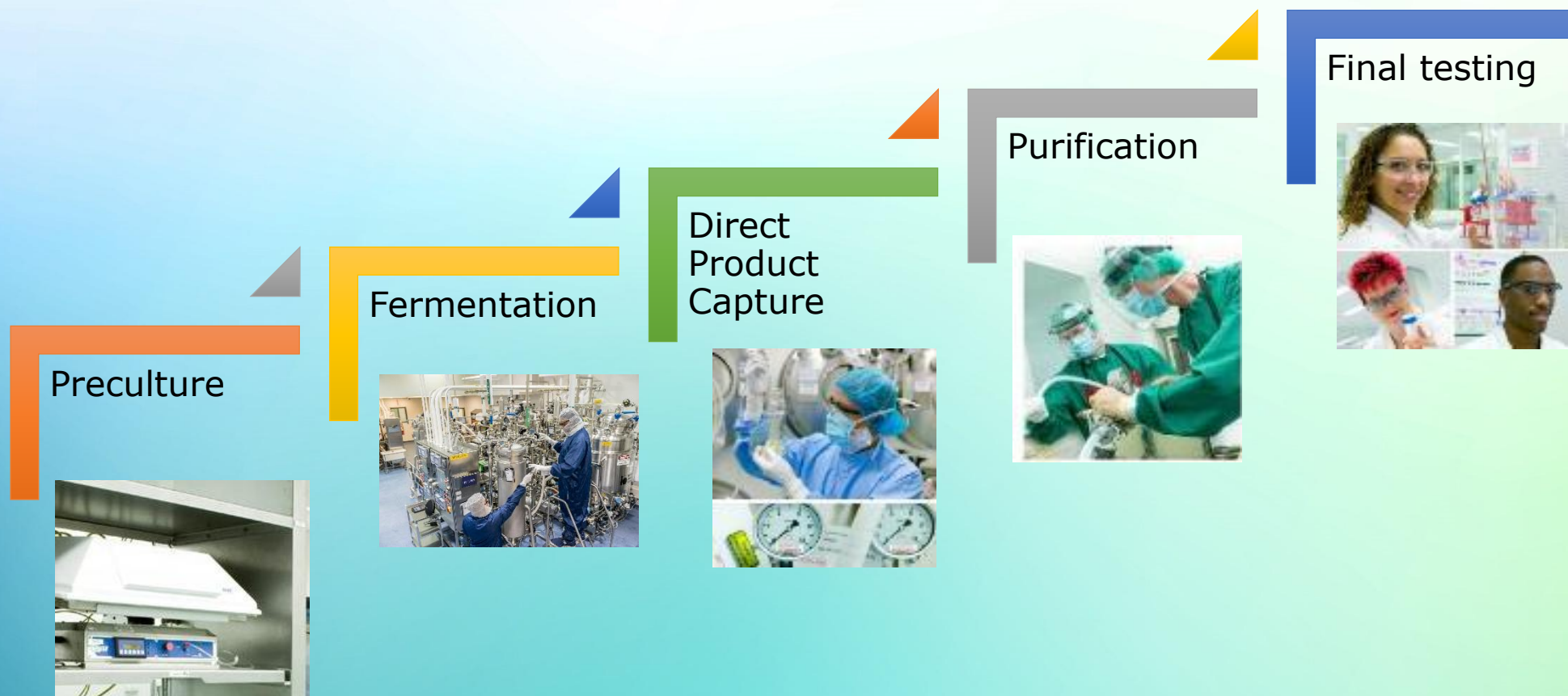
I need to analyze all this process data for cycle time and performance. Where do I start?

Plant Manager

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I need visibility on energy usage! 150 Electrical meters, that a lot of data gathering!

General process flow of Monoclonal antibody production



General process flow of Monoclonal antibody production

Fermentation

Final testing

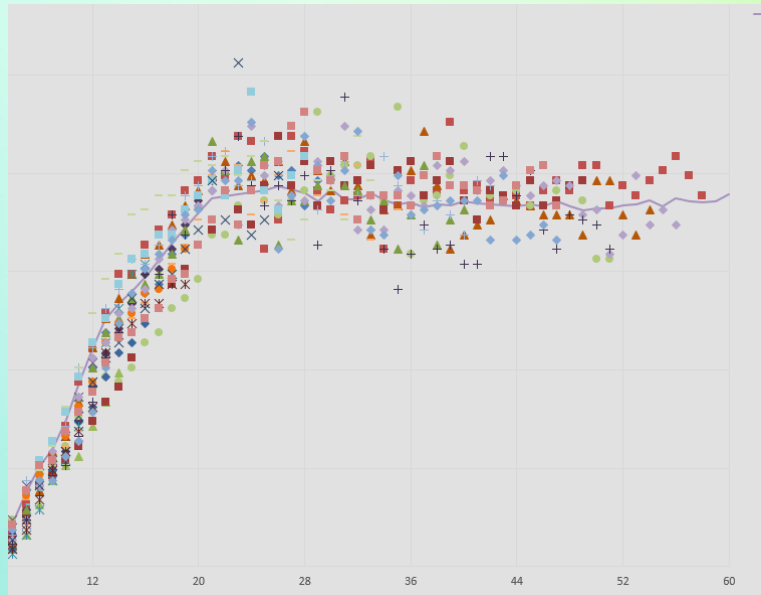
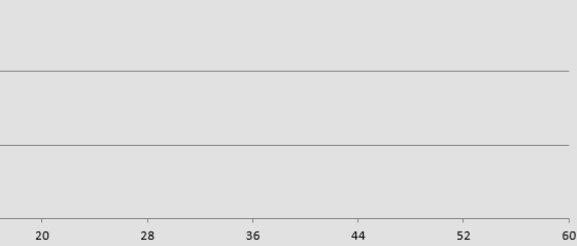
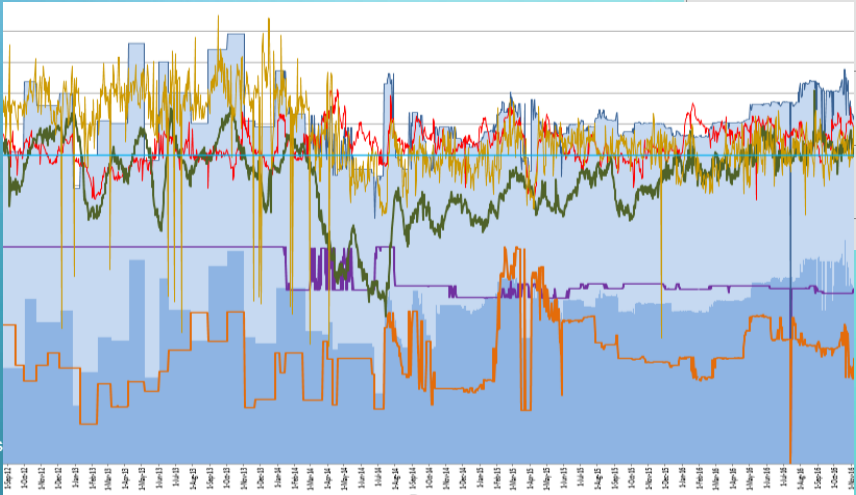
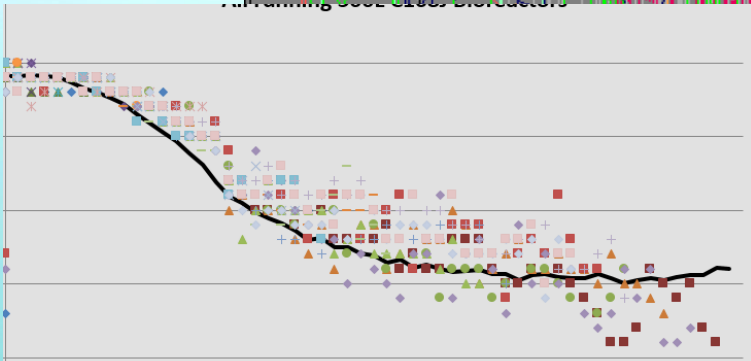
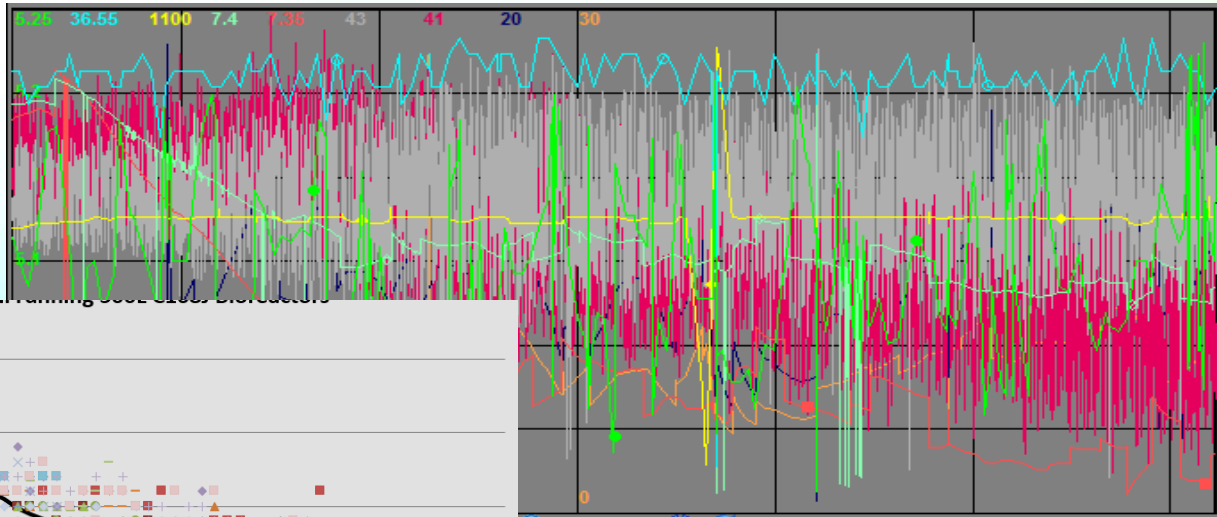
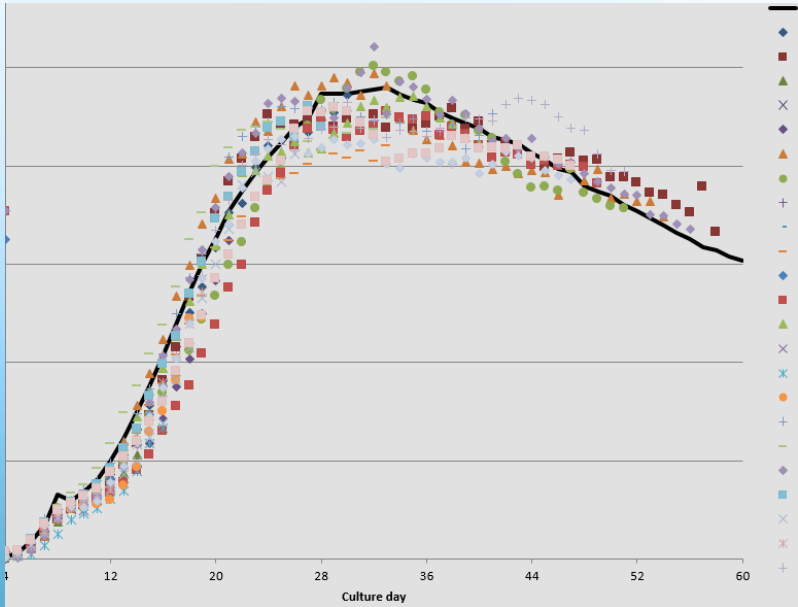
Purification

Preculture

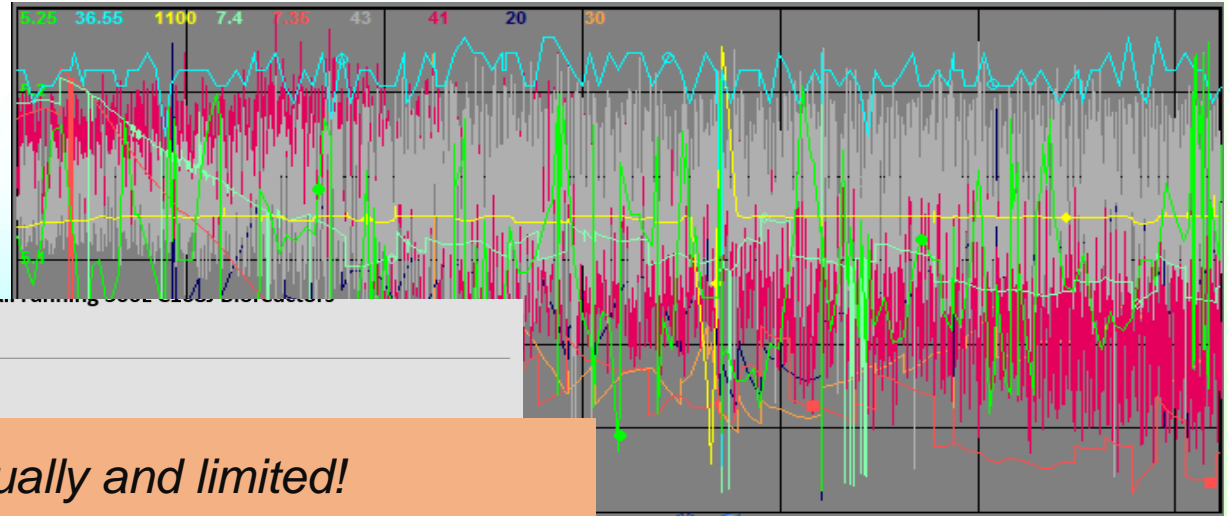
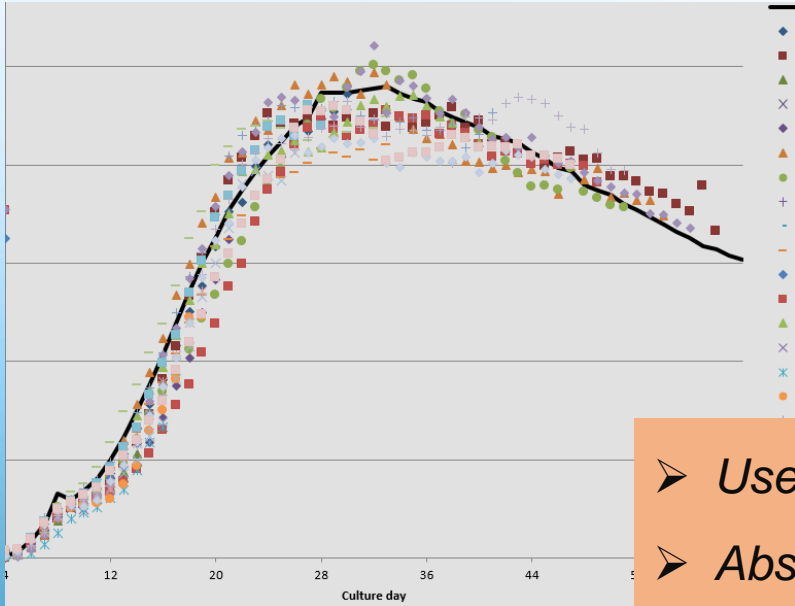


>50 parameters online
>15 parameters offline

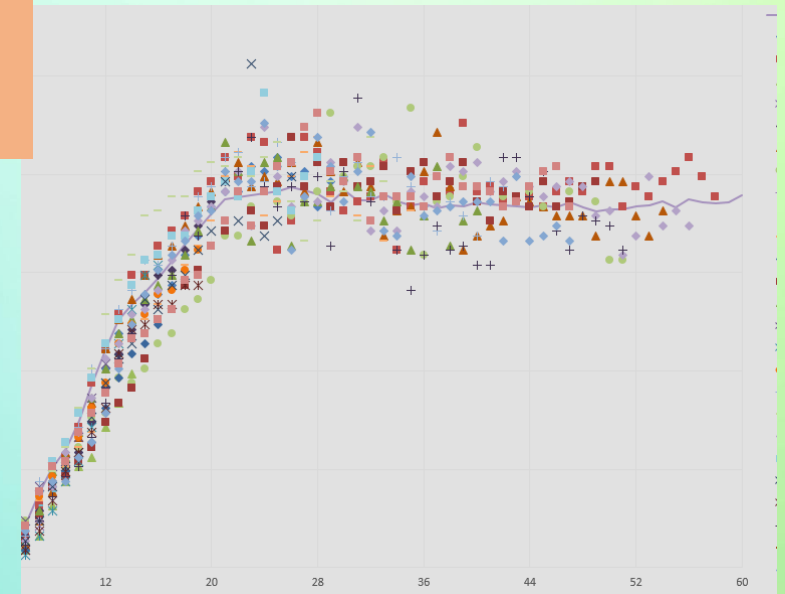
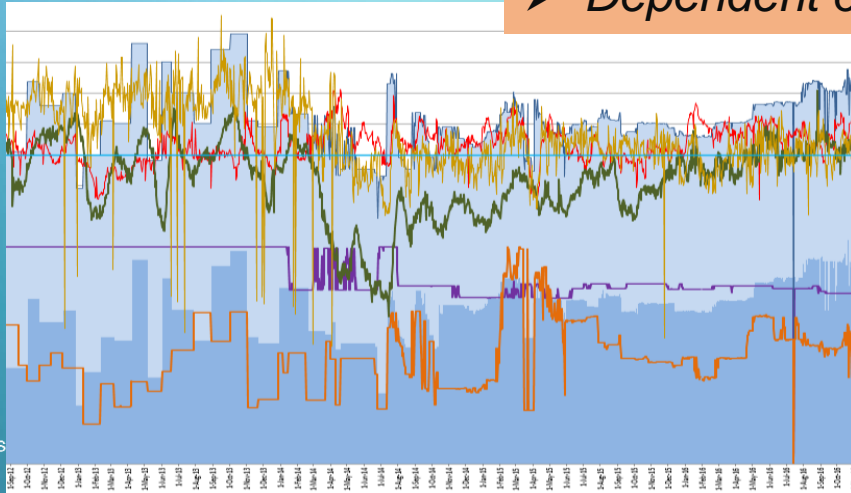
Current way of process monitoring



Current way of process monitoring

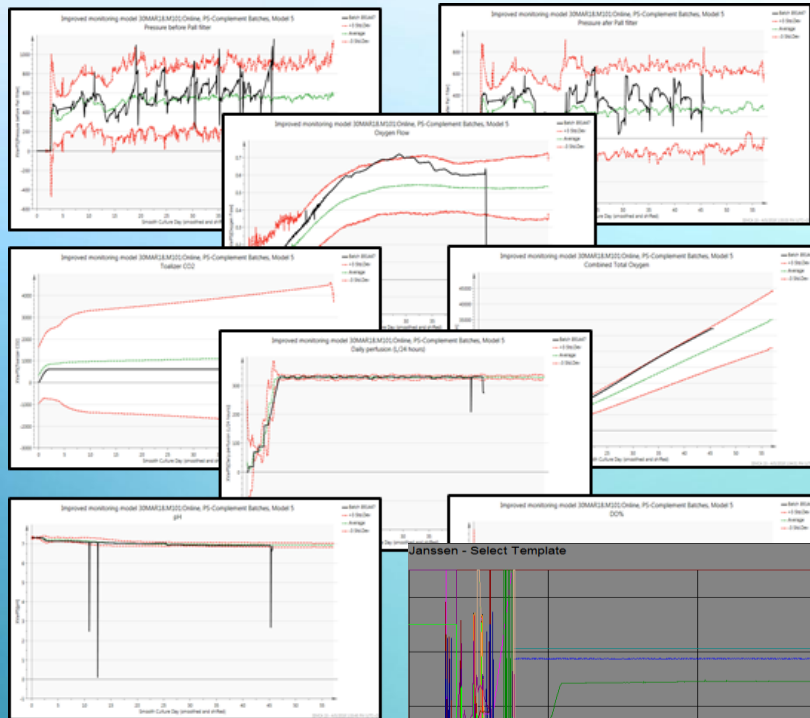


- *Useful but manually and limited!*
- *Absence of correlation between variables*
- *Dependent on experience of engineers*

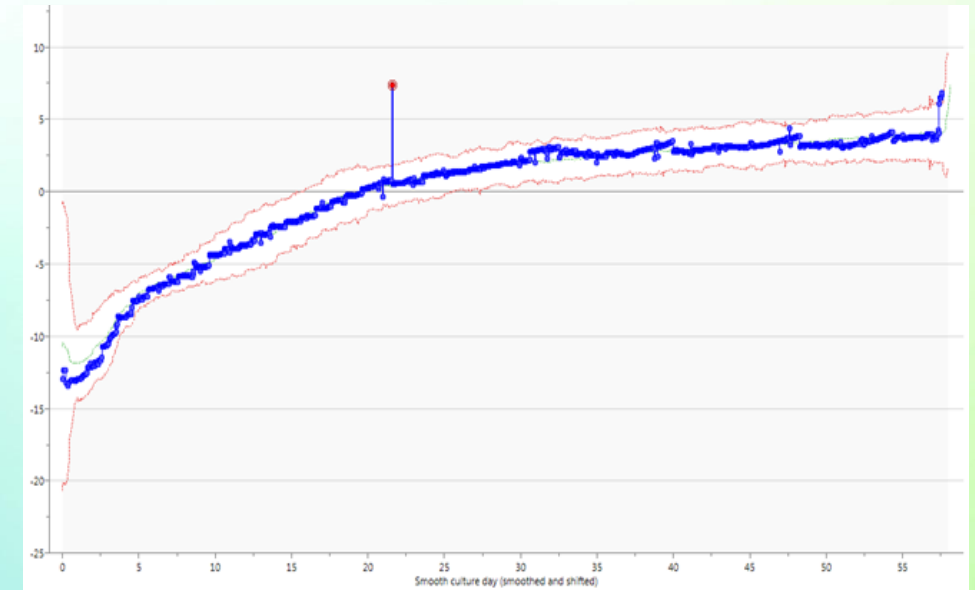
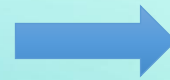


Multivariate Data Analysis

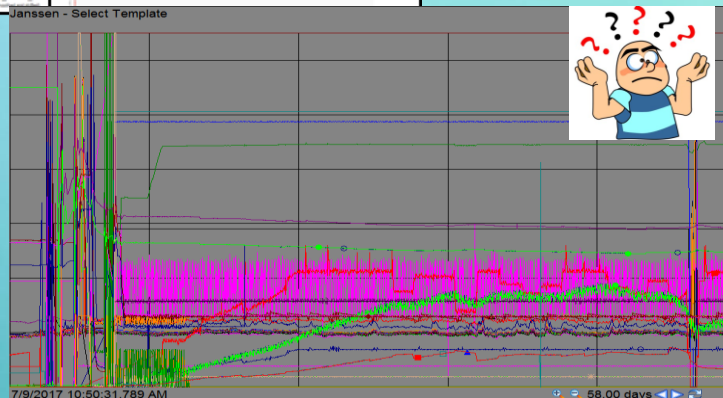
... simply means “the analysis of multiple variables at a time”



Get value out of data

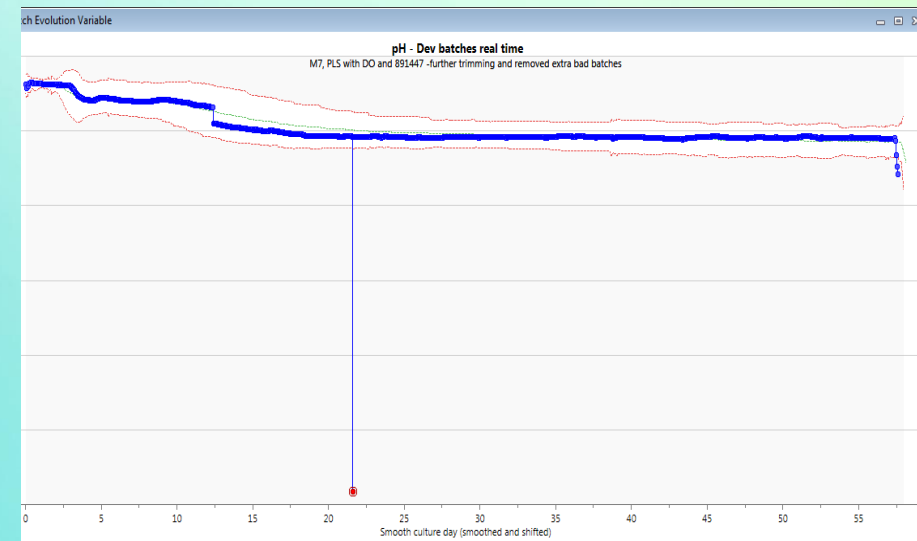
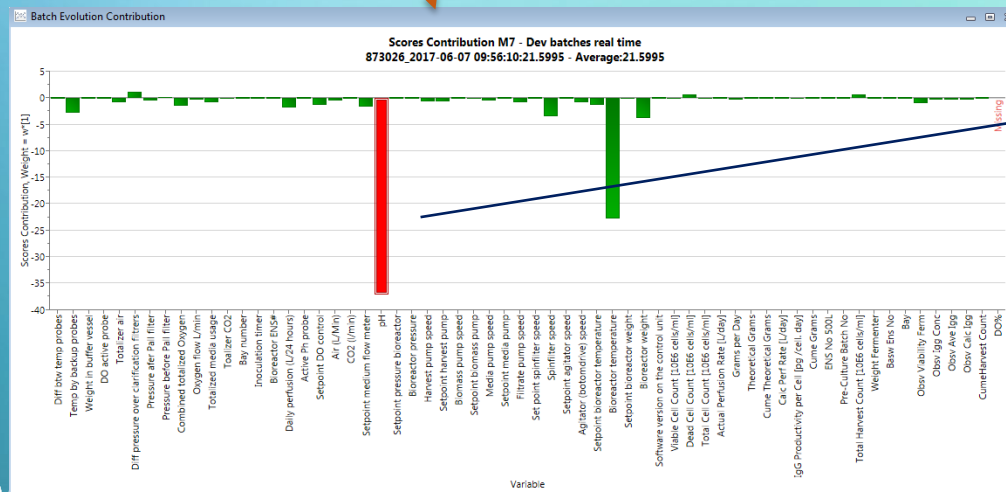
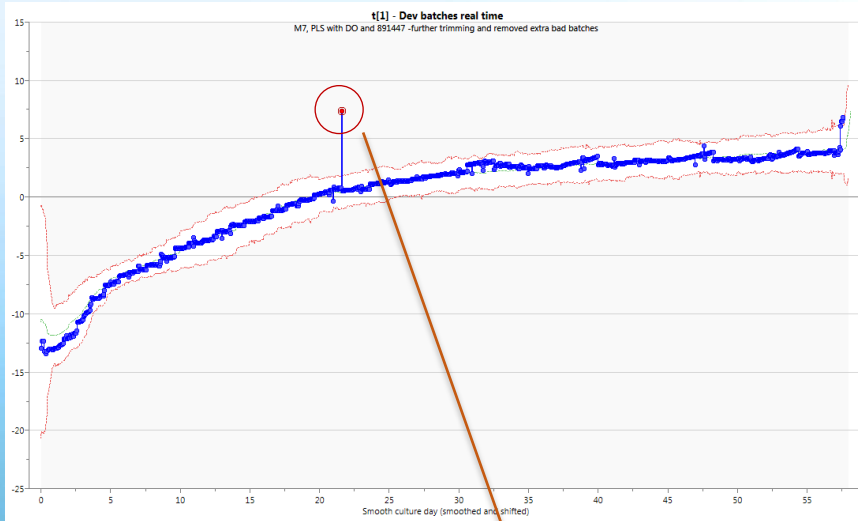


Through MVA, we can create a “summarized” parameter summarizing all variables that can be monitored in real time.

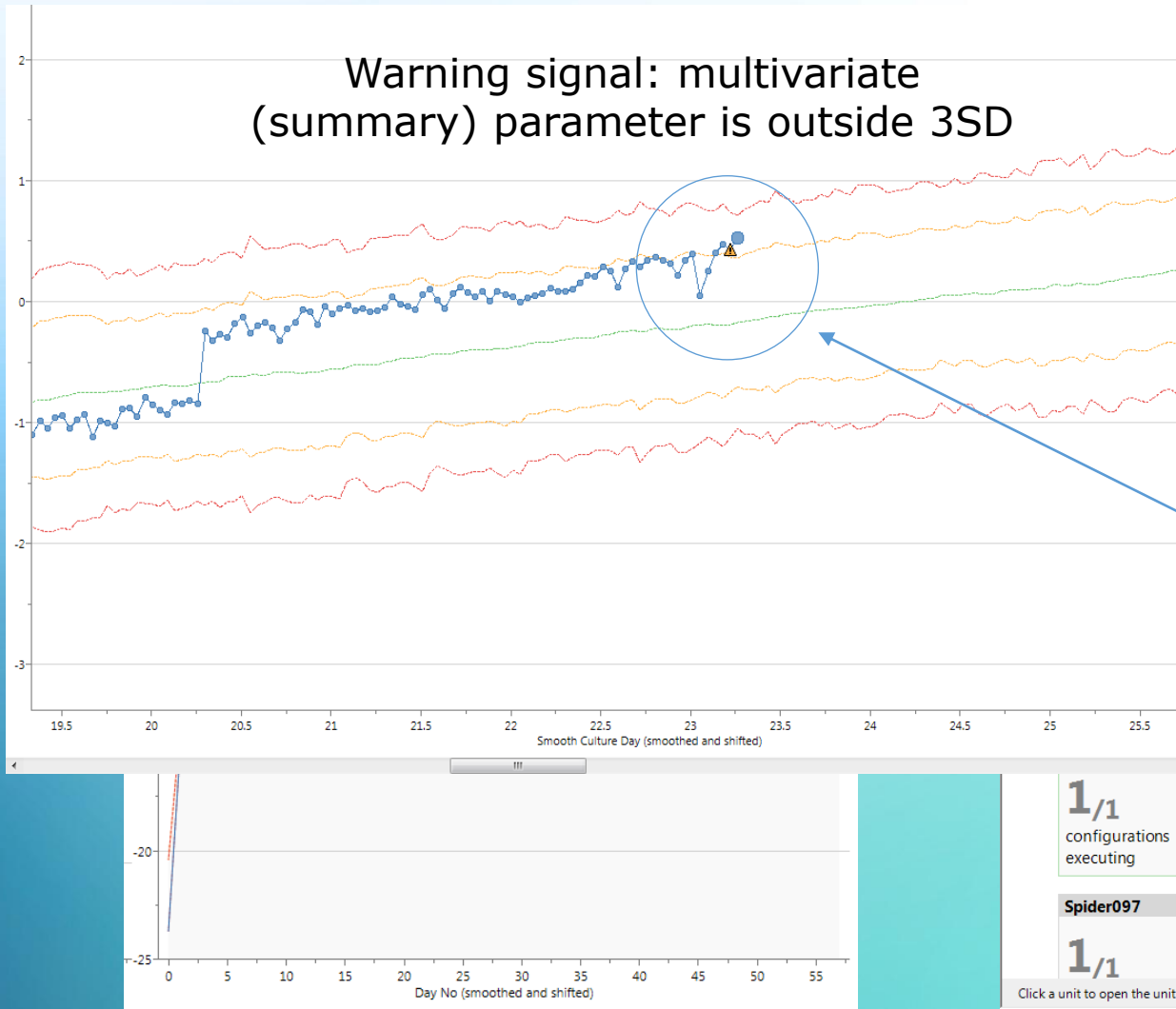


MVA with PI data and SIMCA-online:

- ✓ 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

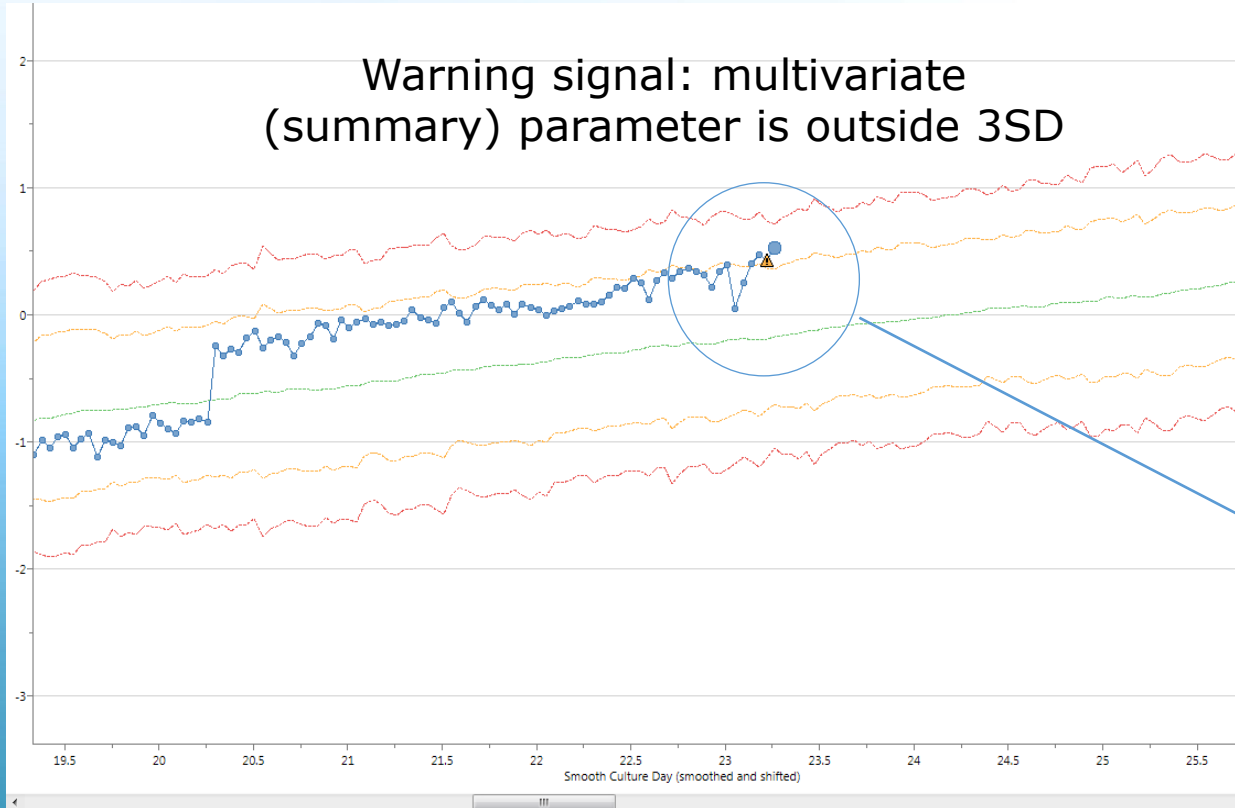


Warning	configurations executing	Warning	configurations executing	configurations executing	configurations executing	Warning
Critical	Spider058 2/4 configurations executing OK	Spider059 1/1 configurations executing Warning	Spider060 1/1 configurations executing N/A	Spider061 1/1 configurations executing OK		
N/A	Spider065 1/1 configurations executing N/A	Spider066 1/1 configurations executing OK	Spider068 1/1 configurations executing OK	Spider069 1/1 configurations executing OK		
OK	Spider073 1/1 configurations executing OK	Spider074 1/2 configurations executing N/A	Spider075 1/1 configurations executing N/A	Spider077 1/1 configurations executing N/A		
	Spider081 1/1 configurations executing OK	Spider082 1/1 configurations executing N/A	Spider083 1/1 configurations executing Warning	Spider096 2/4 configurations executing OK		
	Spider097 1/1 configurations executing N/A	Spider01A 0/1 configurations executing N/A				

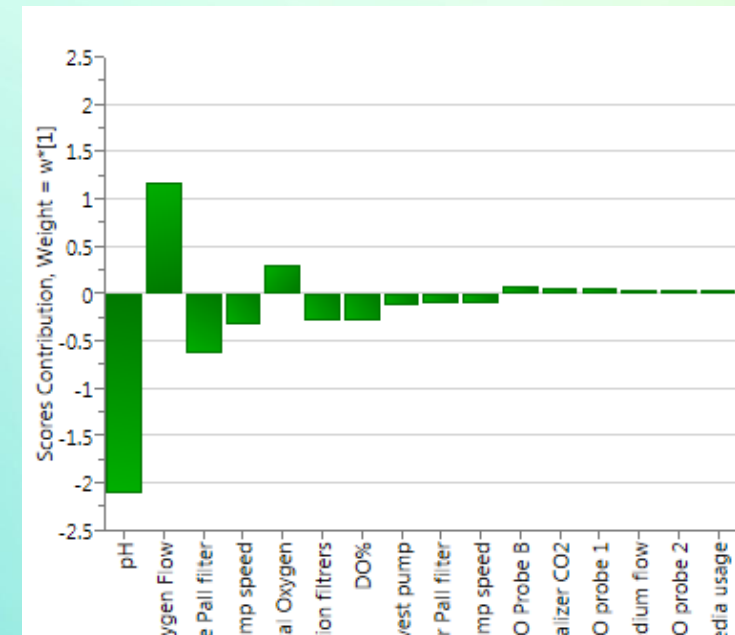
Click a unit to open the unit related configurations.

Warning signal on spider 83!

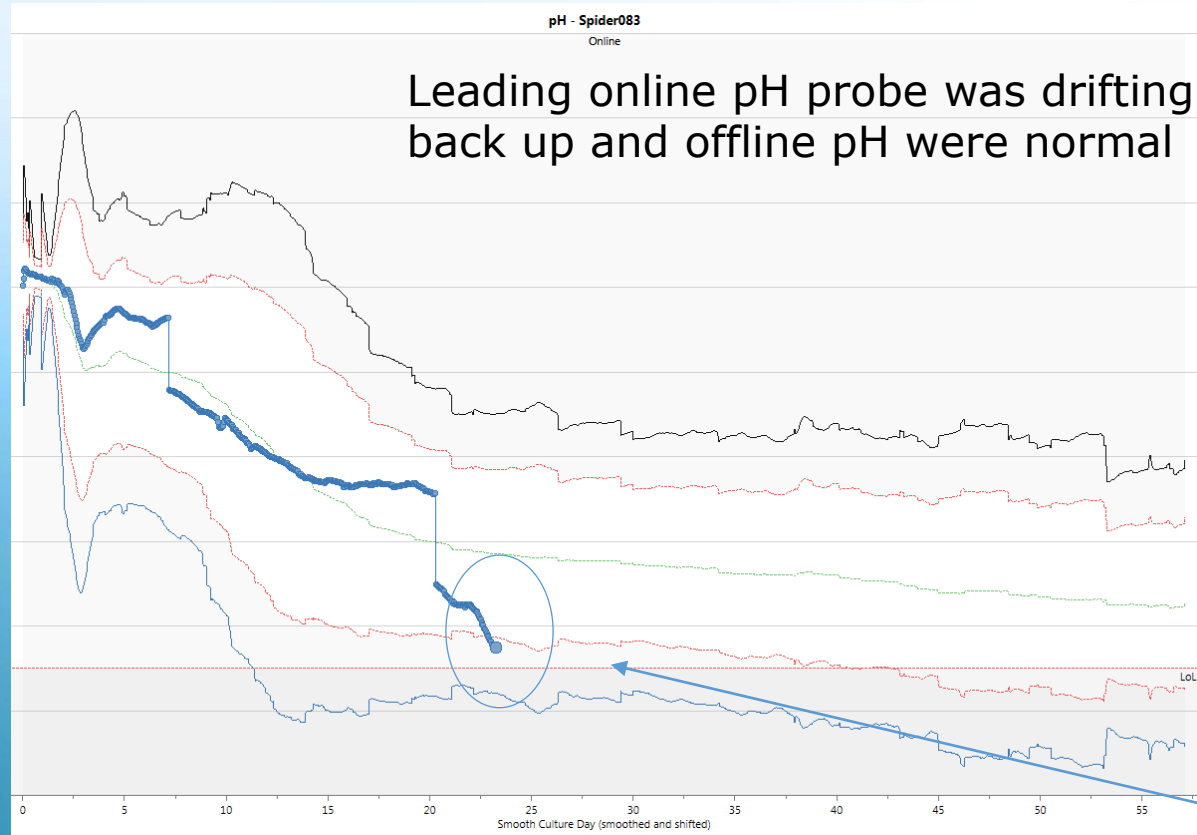
Examples on useful MVA signals: Online pH probe drifting



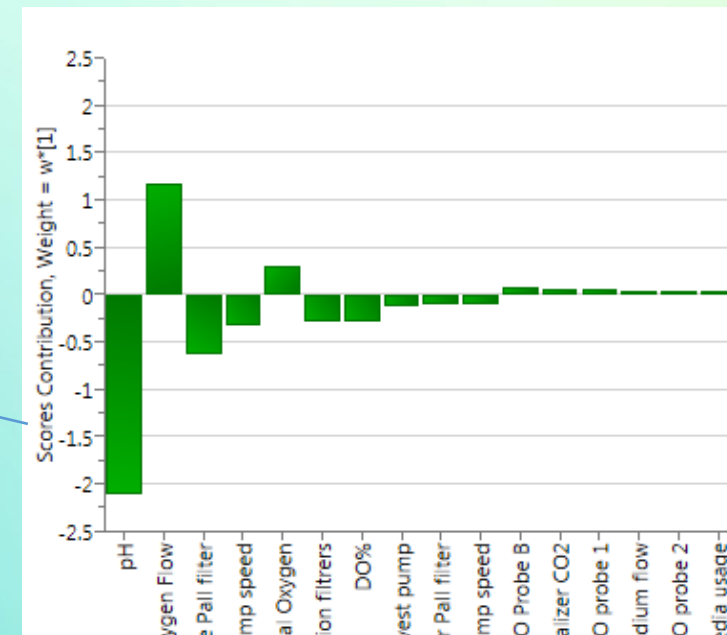
Signal related to low pH, high O2 flow...



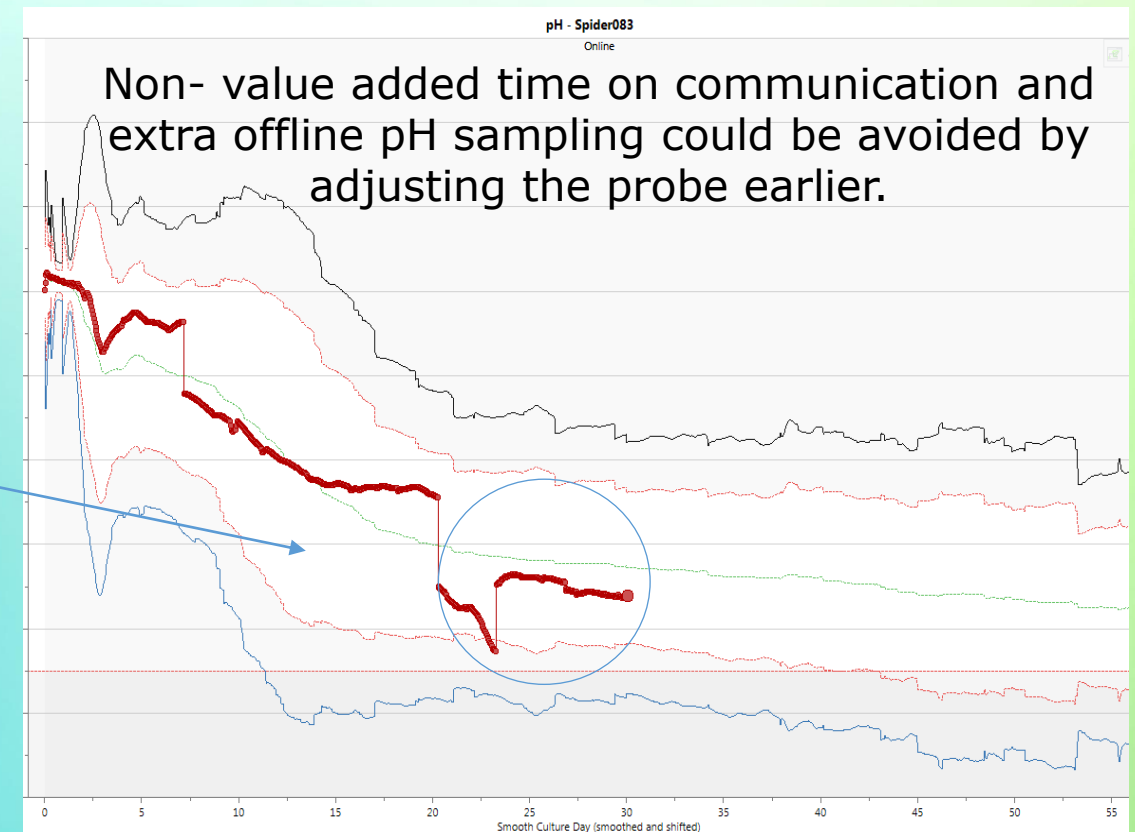
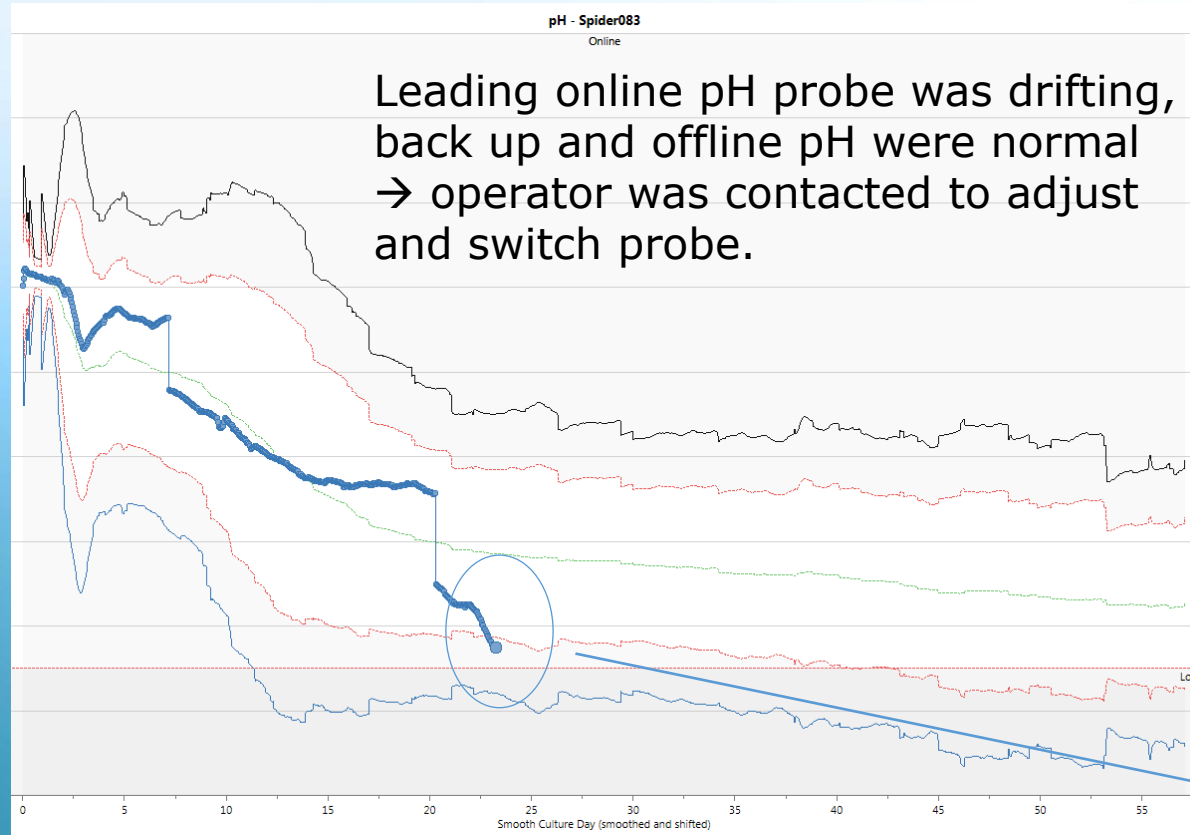
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Signal related to low pH, high O2 flow...

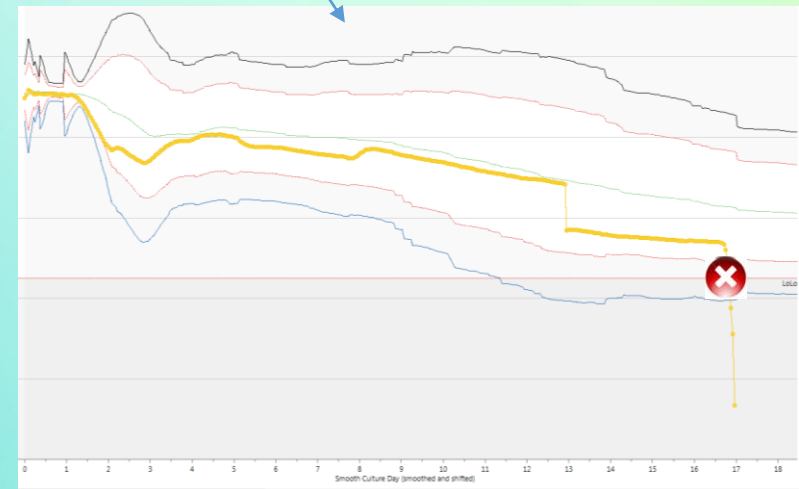
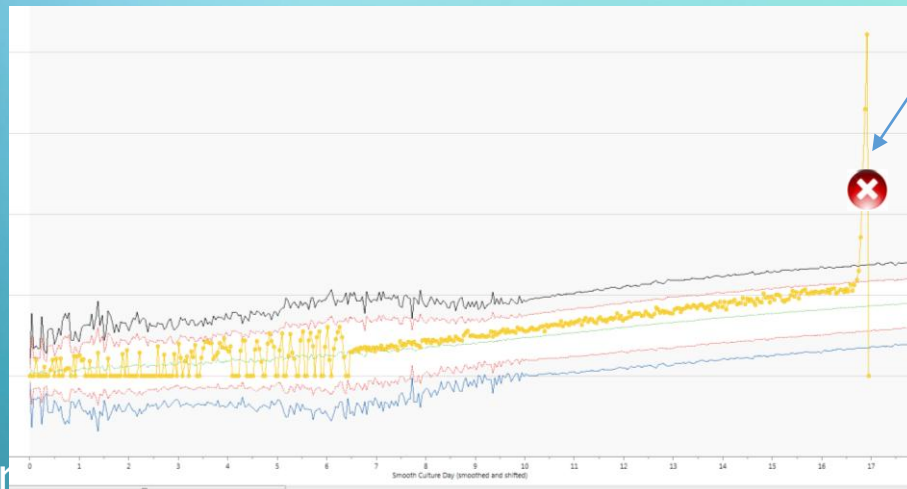
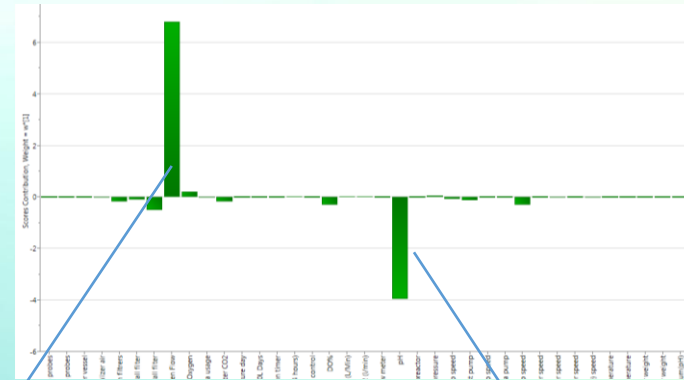
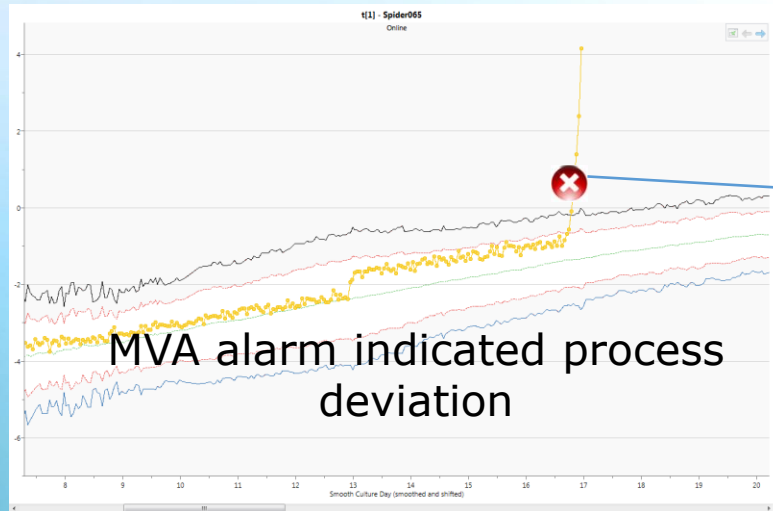


Examples on useful MVA signals: Online pH probe drifting

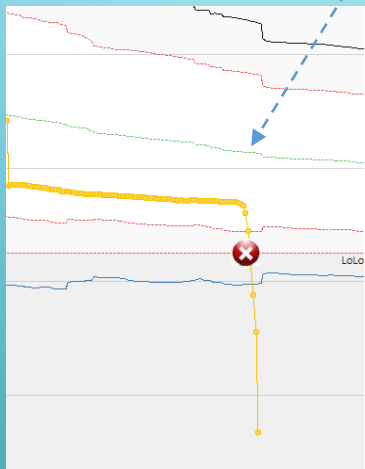
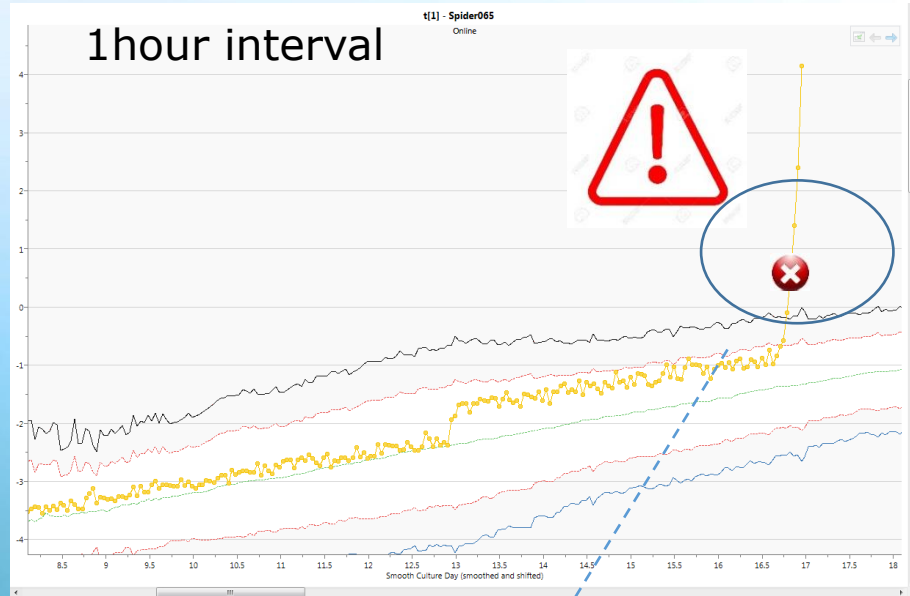


Examples on useful MVA signals: Contamination early detection

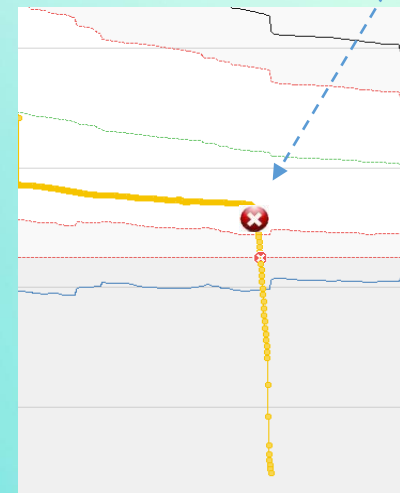
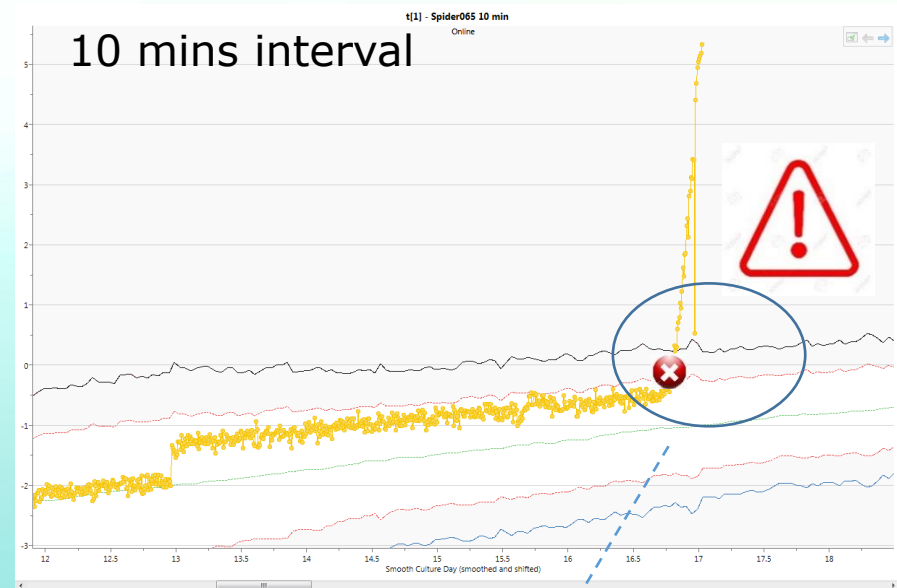
BRX 500L contamination: pH dropped and DO increased quickly.



Examples on useful MVA signals: Contamination early detection

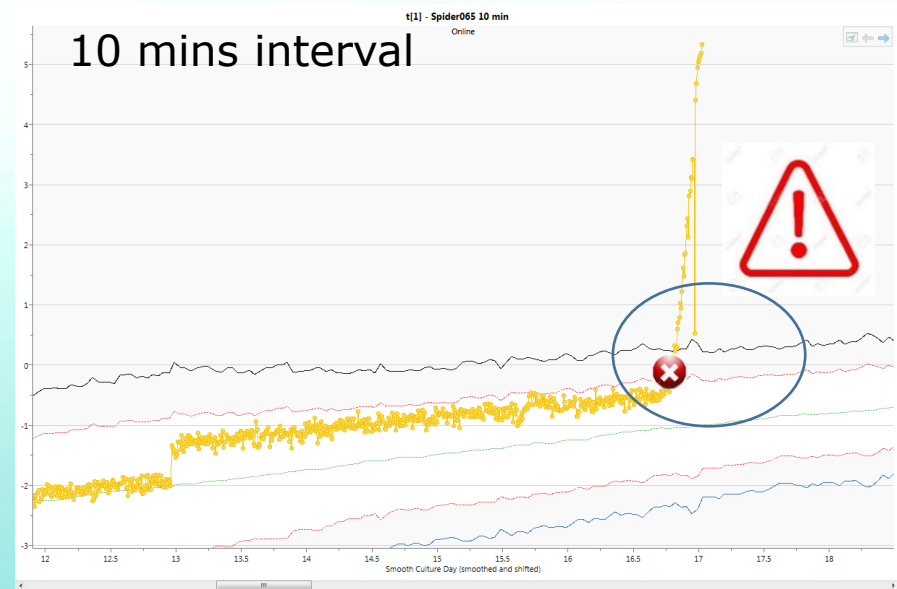
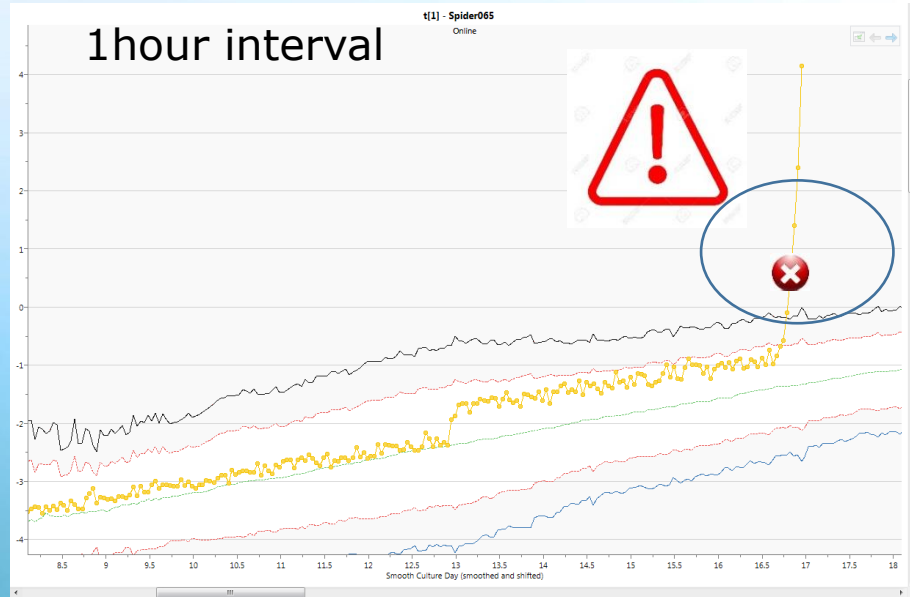


Warning at the same time of out of specification alarm



Warning 2 hrs before pH dropped to lower specification limit

Examples on useful MVA signals: Contamination early detection



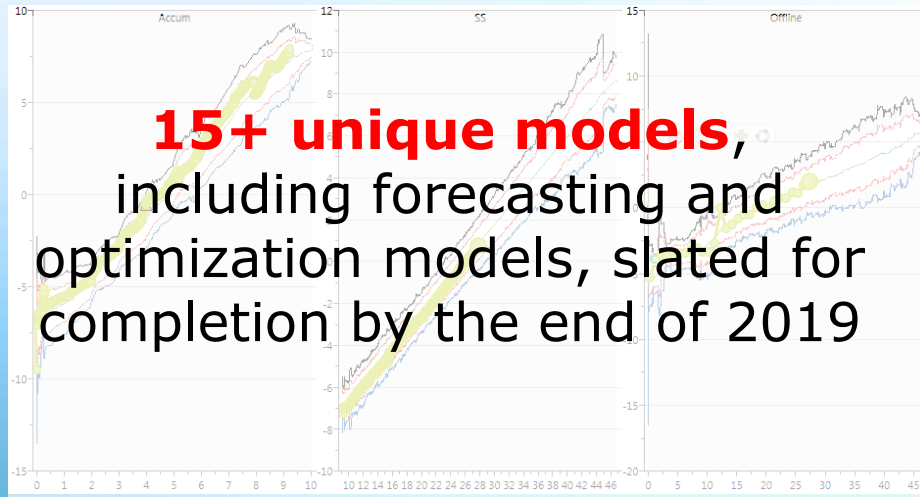
Although the MVA (10min interval) cannot prevent the contamination, it can give early warning, which could help preventing pooling the contaminated harvests to the non-contaminated ones, leading to saving up to 1 DPC batch (~€200k).

Deployment of SIMCA-online at Janssen Globally

(*Prometheus*)



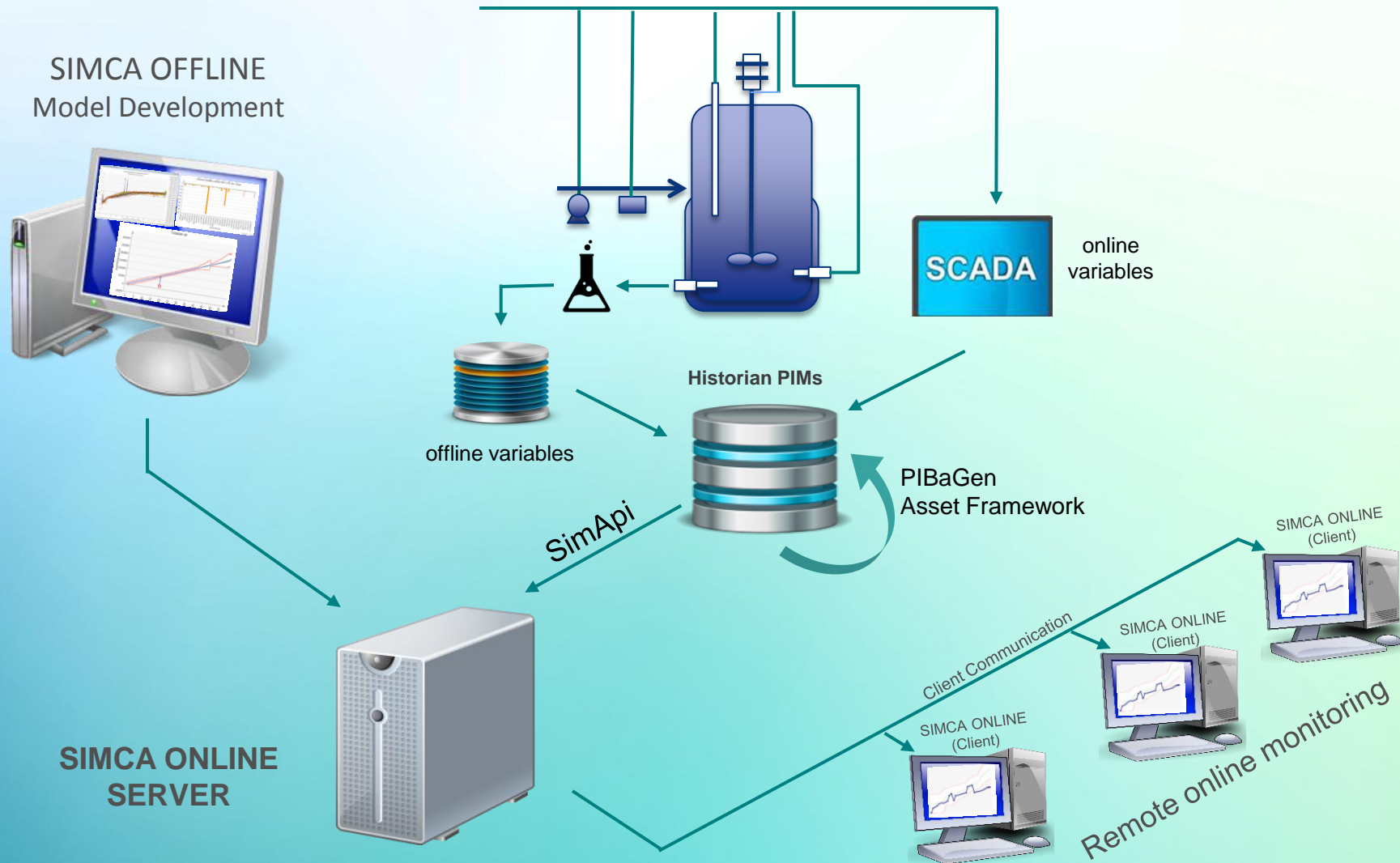
Deployment of SIMCA-online at Janssen Globally



RTMVA path forward



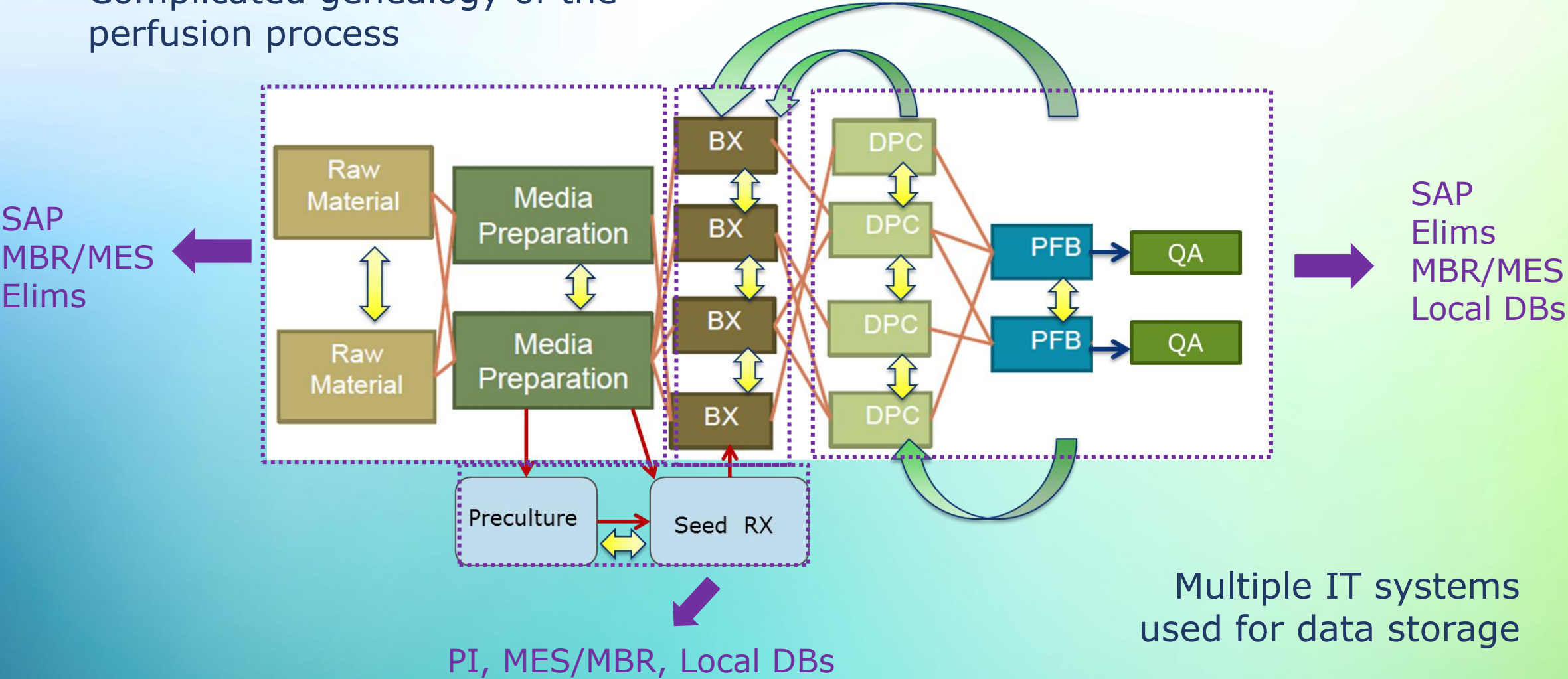
How was PI - SIMCA online server set up?



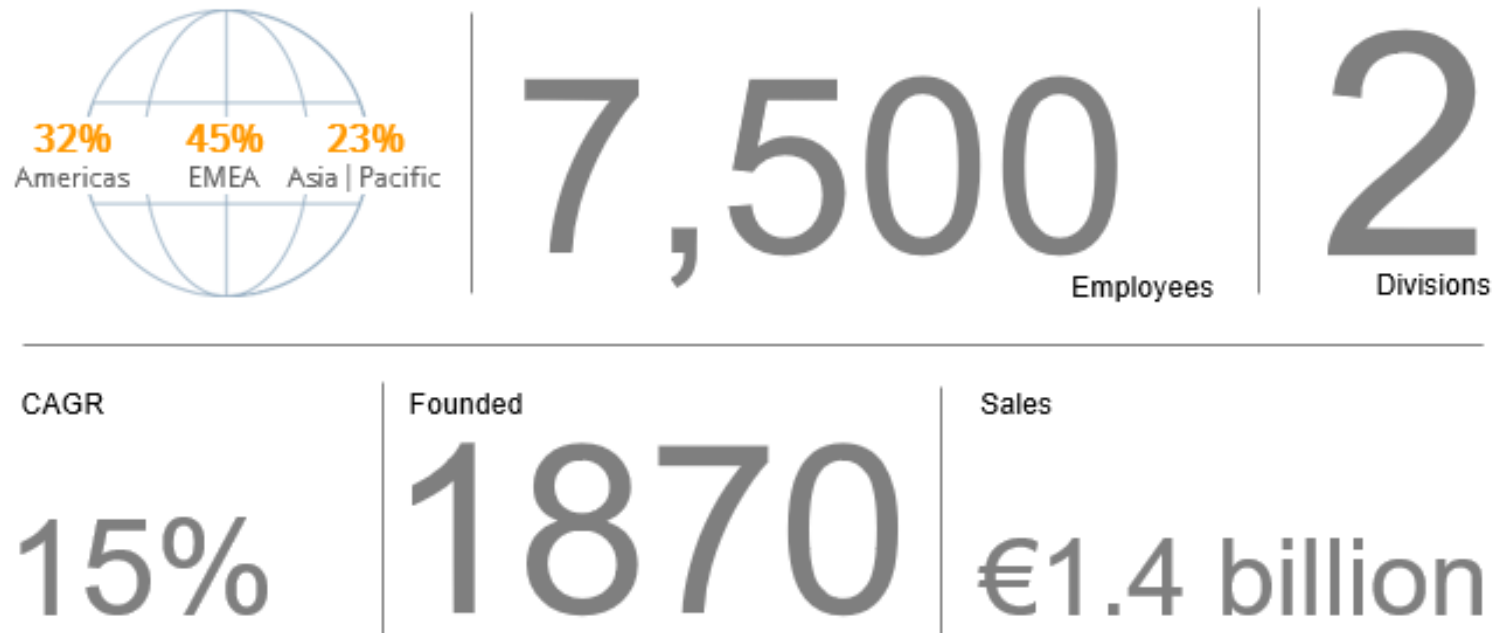
Scientist
Engineer
Team lead
Operator

Challenges

Complicated genealogy of the perfusion process



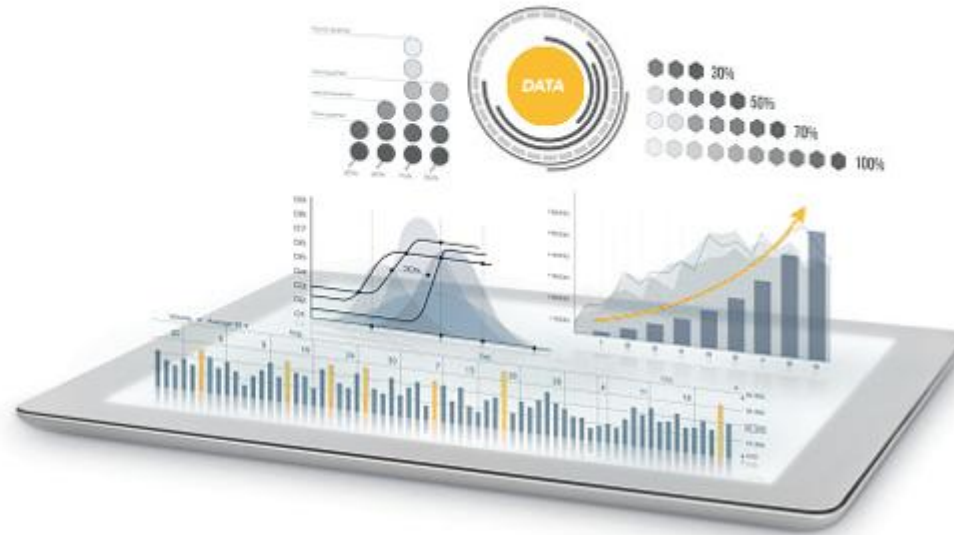
Sartorius at a glance



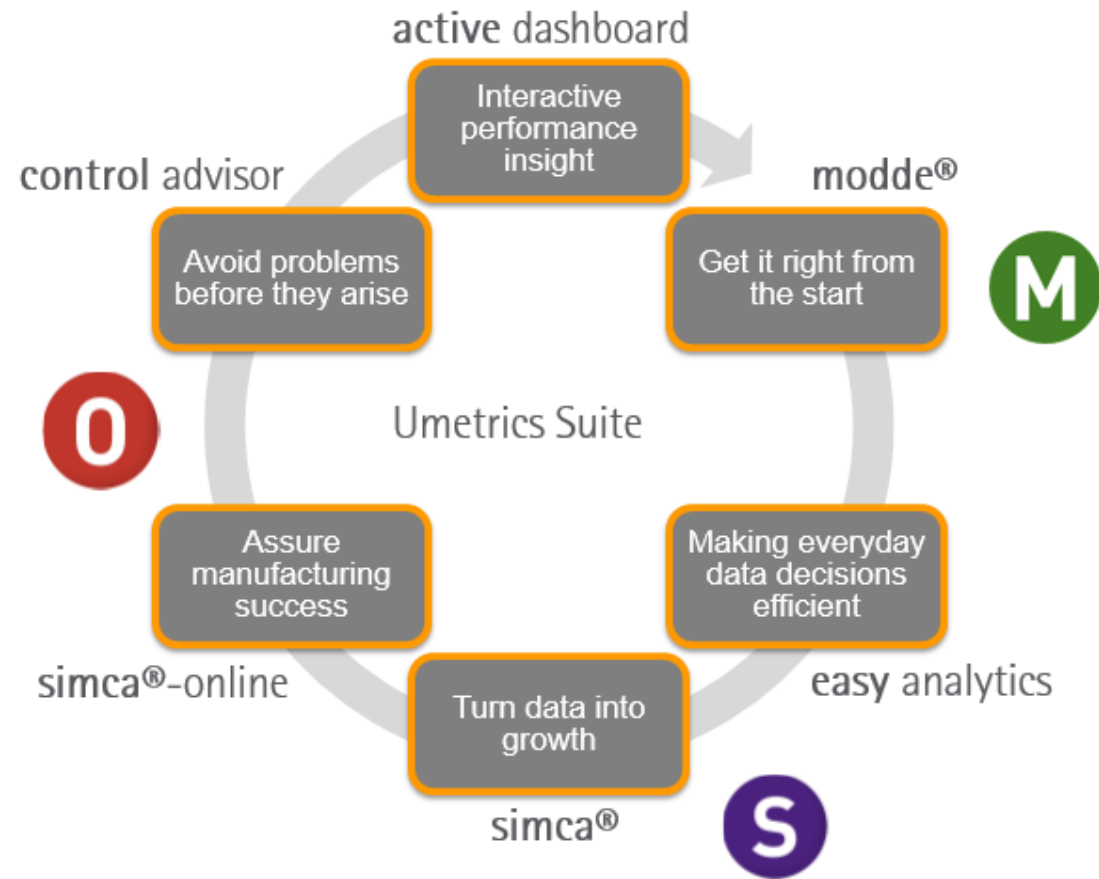
Sartorius Stedim Data Analytics

- 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

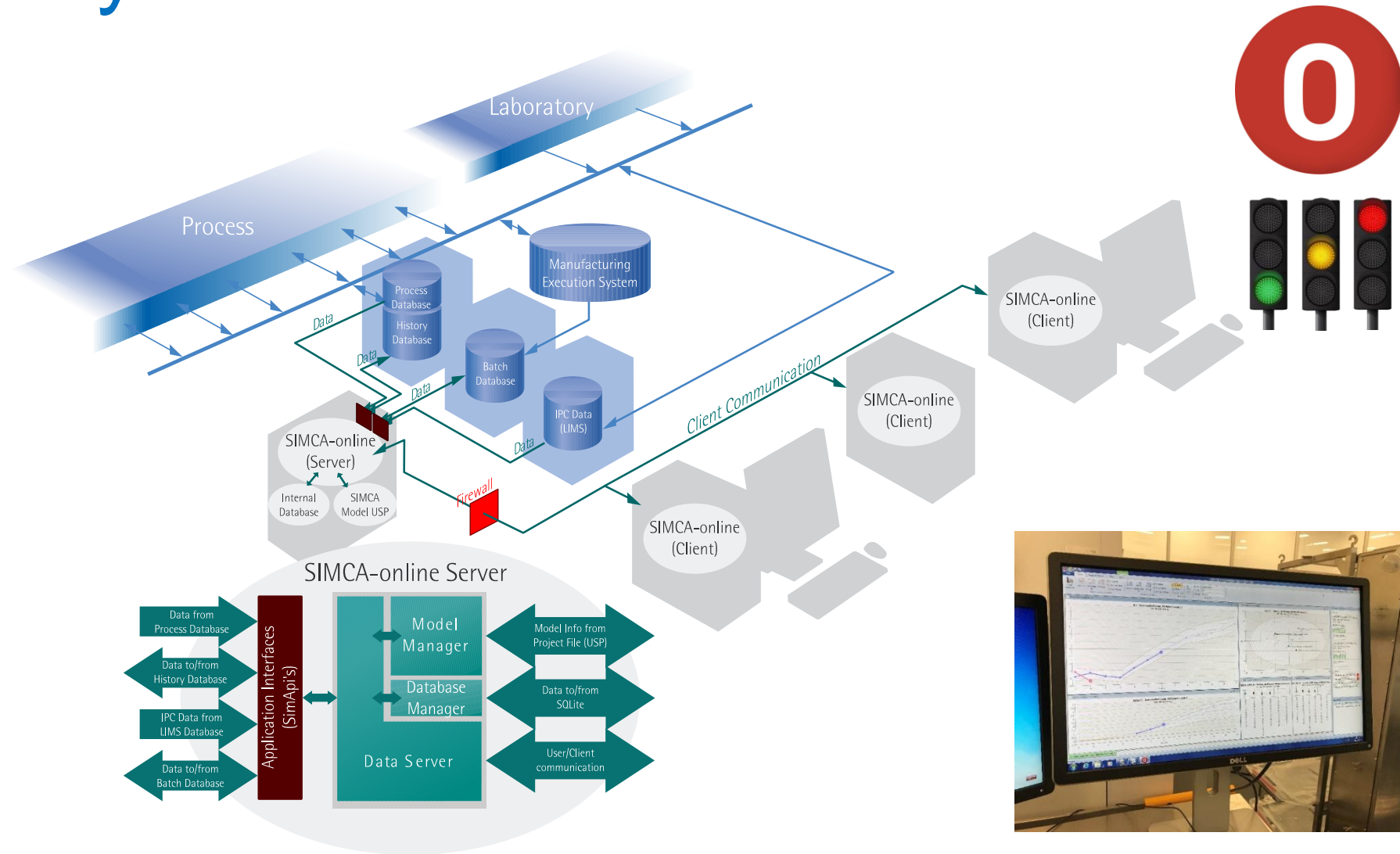
Enabling our customers to see
what others don't



Umetrics™ Suite of Data Analytics Solutions

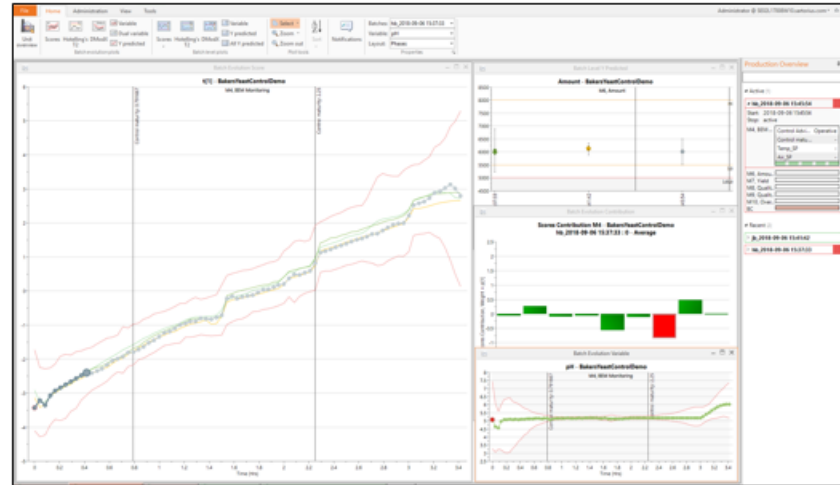


Deployment: SIMCA-online

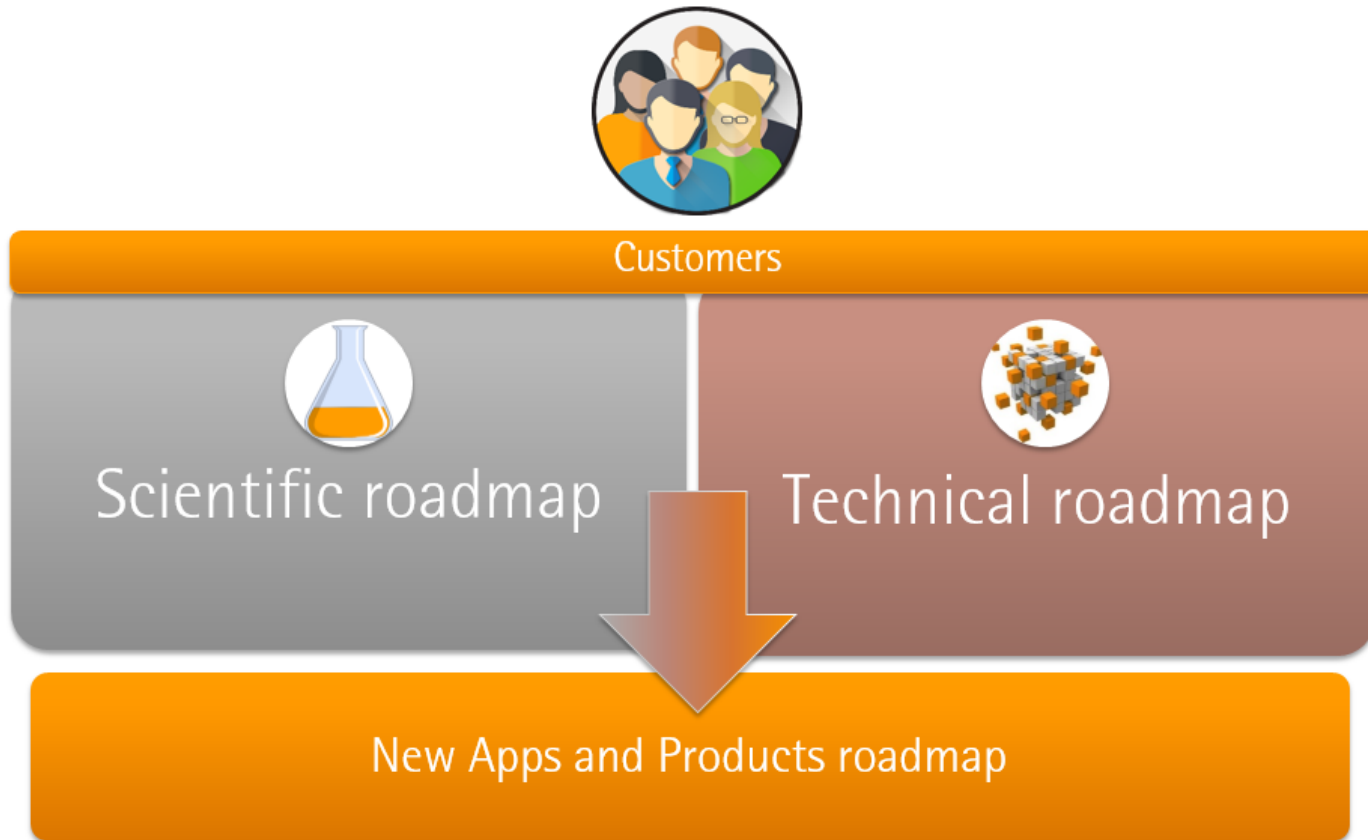


What can SIMCA[®]-online do on top of OSI PI AF

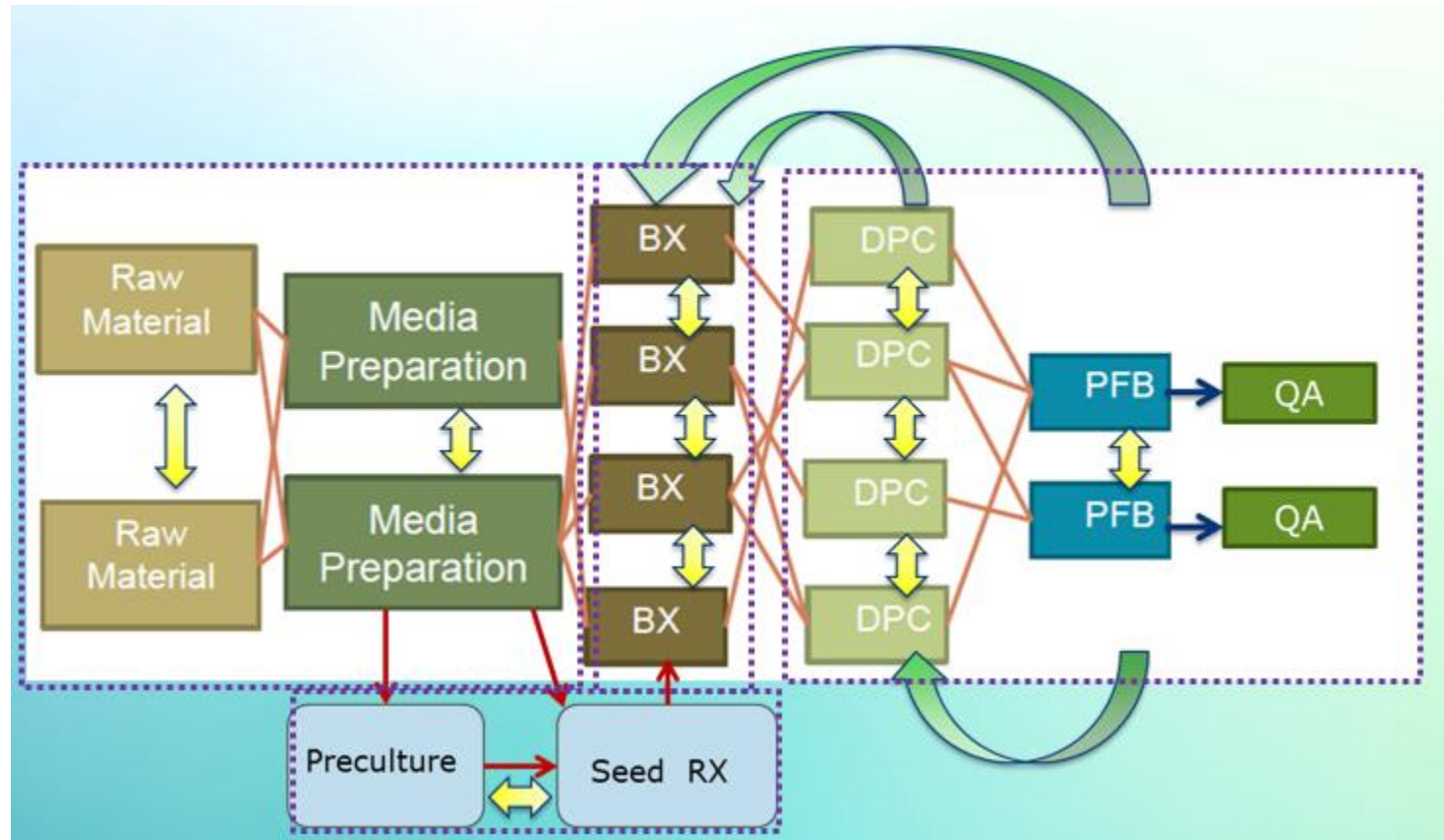
- Monitoring of "Golden batch"
- Forecasts of "what will happen"
- Stable production advisor
- Process improvements
- Soft sensor of final product quality
- Root cause investigation
- Ahead of time fault investigations



Umetrics® Suite roadmaps

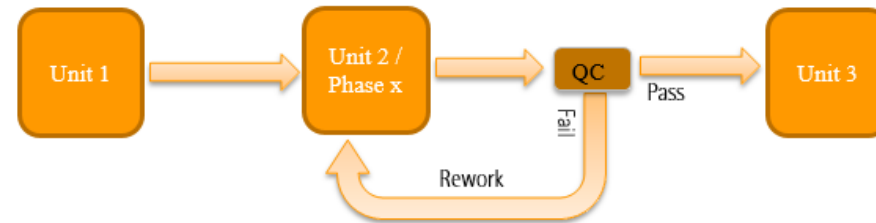


Janssen challenge

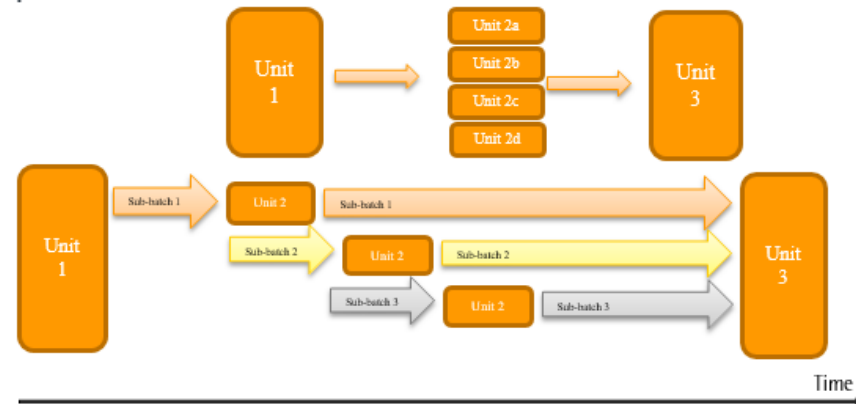


Recurrence of batches and phases

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

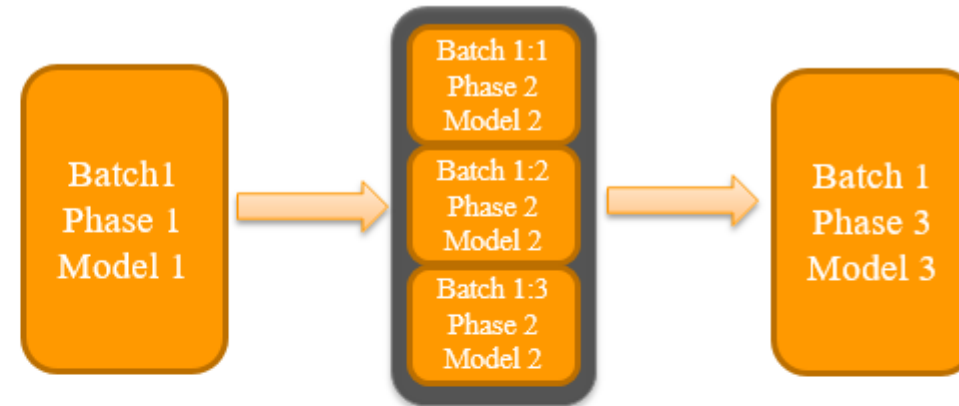


- Batch divided into separately processed sub-batches
 - Complex genealogy



Customer challenges addressed

- Recurring phases in upstream and downstream processing

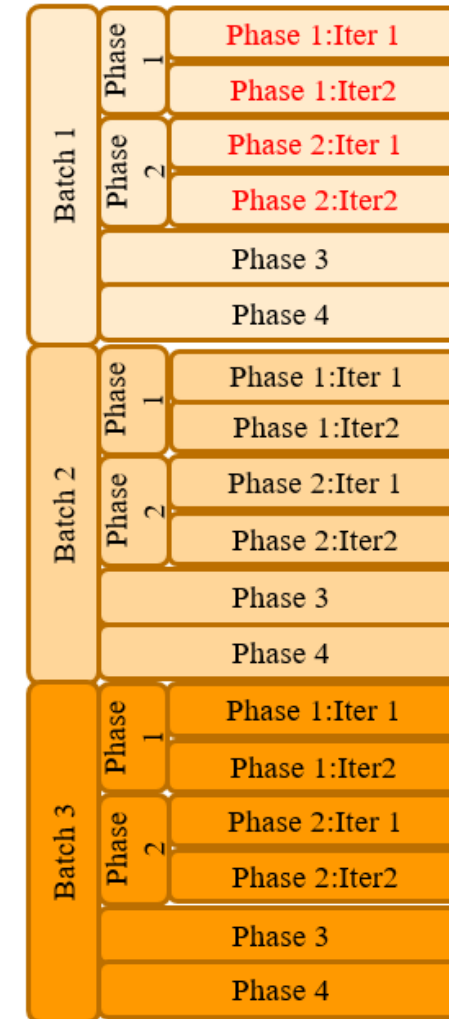
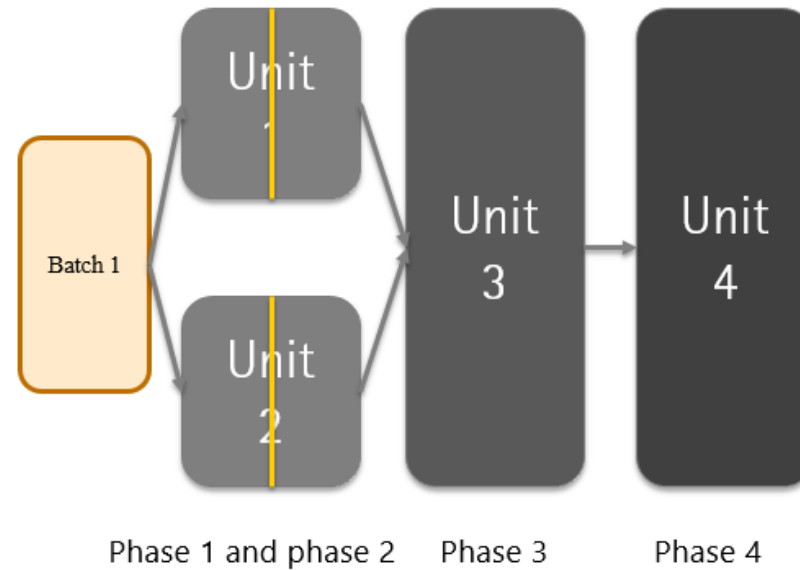


- Ability to combine all data for the batch
 - CPV
 - Quality/output prediction
 - Comparing unit performance



Data Structure requirements

Hierarchy: Batch, phase, phase iteration



Batch phase iterations in SIMCA-online





PHARMACEUTICAL COMPANIES OF
Johnson & Johnson



CHALLENGE

Lack the overview of process variables, leading to undesirable 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

Acknowledgements

Leiden RTMVA

- *Aldo Braam*
- *Martijn Goedhart*
- *Ward Blanken*
- *Snehal Patil*

Coaches/sponsors

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- *Nick Sessa*
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- *Partick O'Sullivan*

Team at Sartorius Stedim Data Analytics

Thank you!



sartorius stedim
biotech

Back up