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QbD
Quality by Design

IFPAC
Process Analytical Technology

QbD
Quality by Design



Considerations for selecting an Advanced Process Optimization System

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Agenda

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What is an advanced process optimization system?

Aggregation and segregation of multiple data sources

Raw data conversion to valuable information

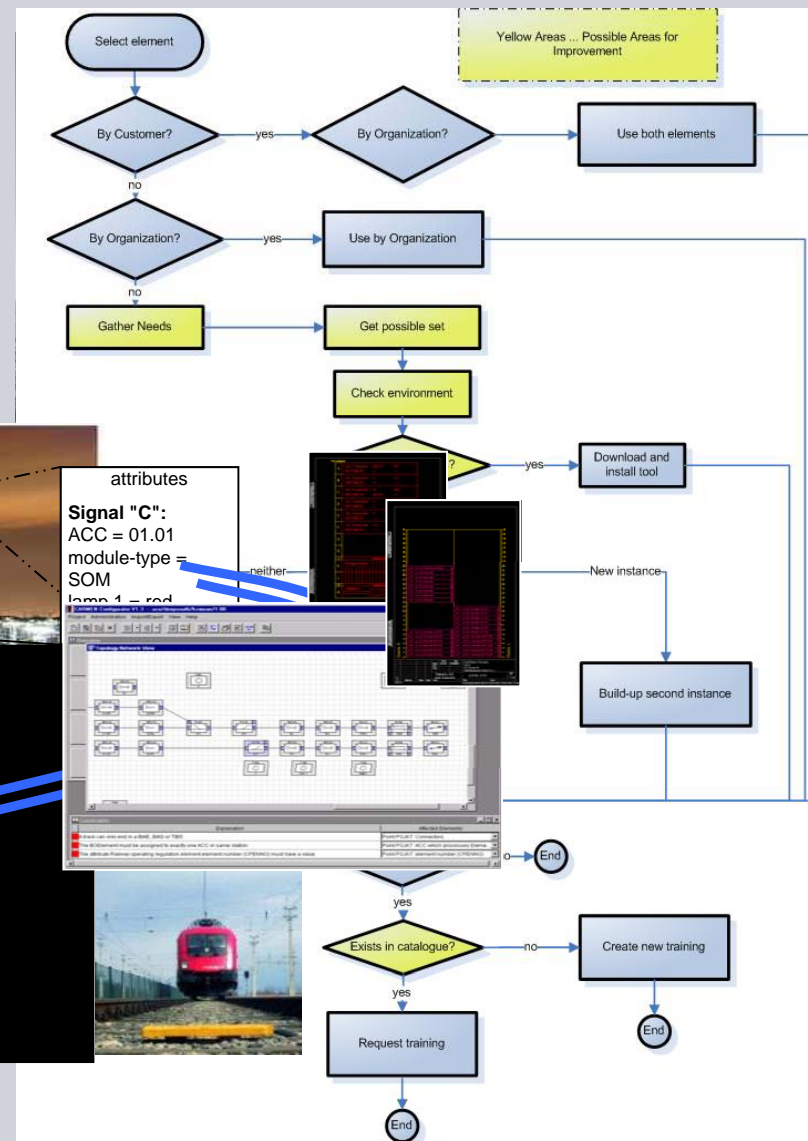
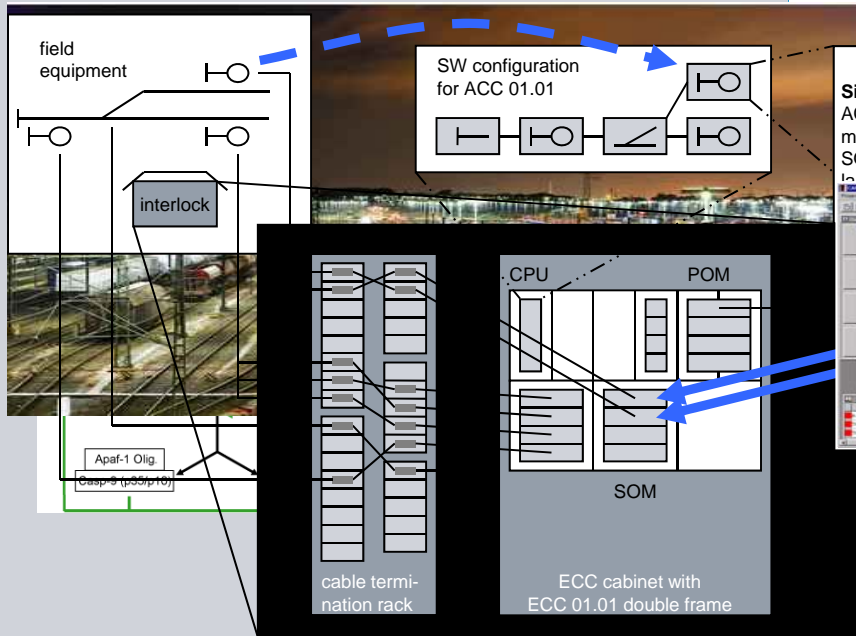
Monitoring & control

Process optimization – getting something back from the system

Modeling of Complex Systems

Typical Modeling Projects

- Wind Park Optimization
- Modeling of Cell Processes
- Business Process Modeling
- Optimizing Constraint Systems



What is an Advanced Process Optimization System?

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Fundamental Aspects:

- Processes
- Advanced Process Control (APC)
- Process Optimization
- System (Manufacturing, Monitoring, Control, ...)

→ Bringing the parts together to provide a solution

Why do process optimization?

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Add business value

Improve product quality

Increase yield

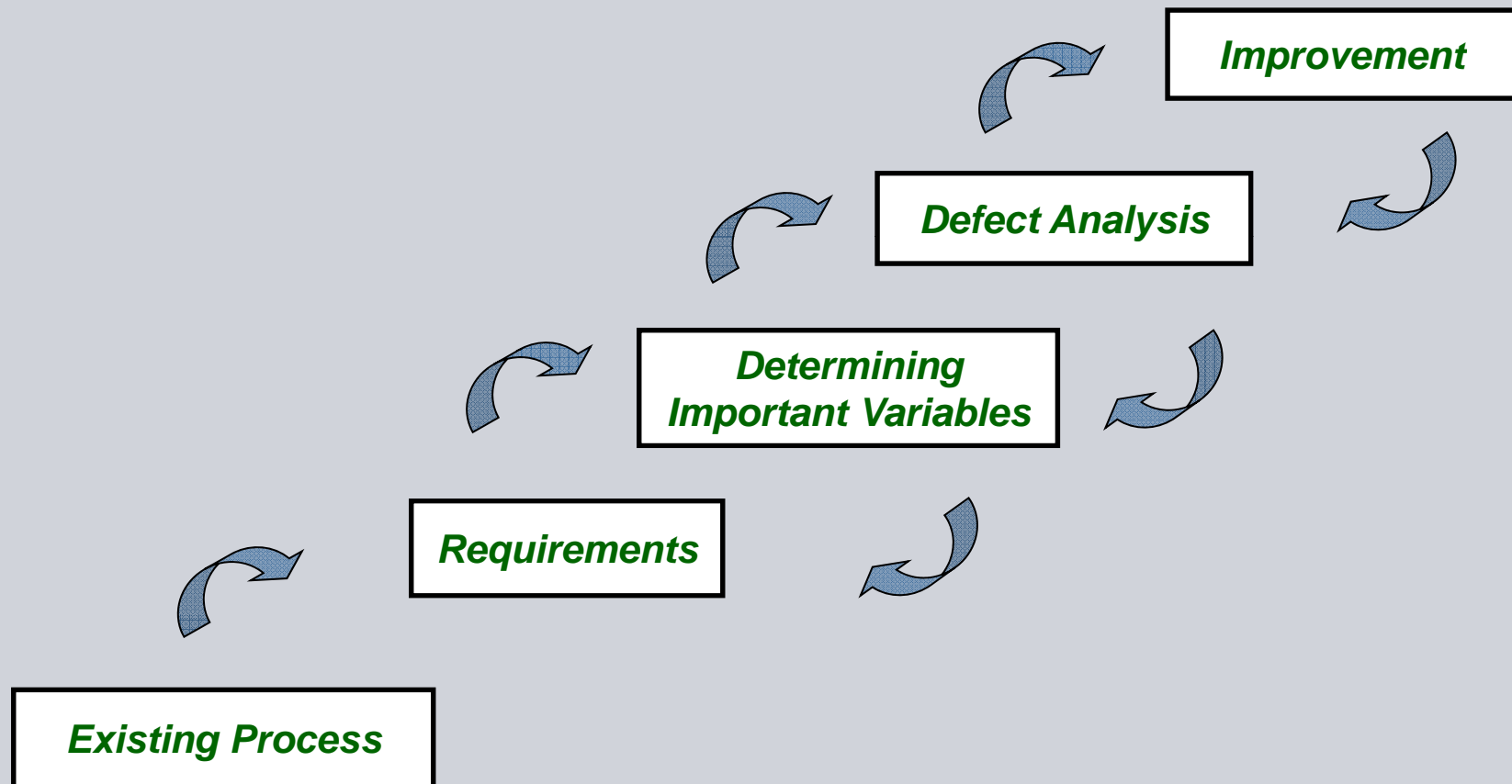
Improve manufacturing efficiency (materials, energy use, resource use...)

Reduce costs (development, materials, resources...)

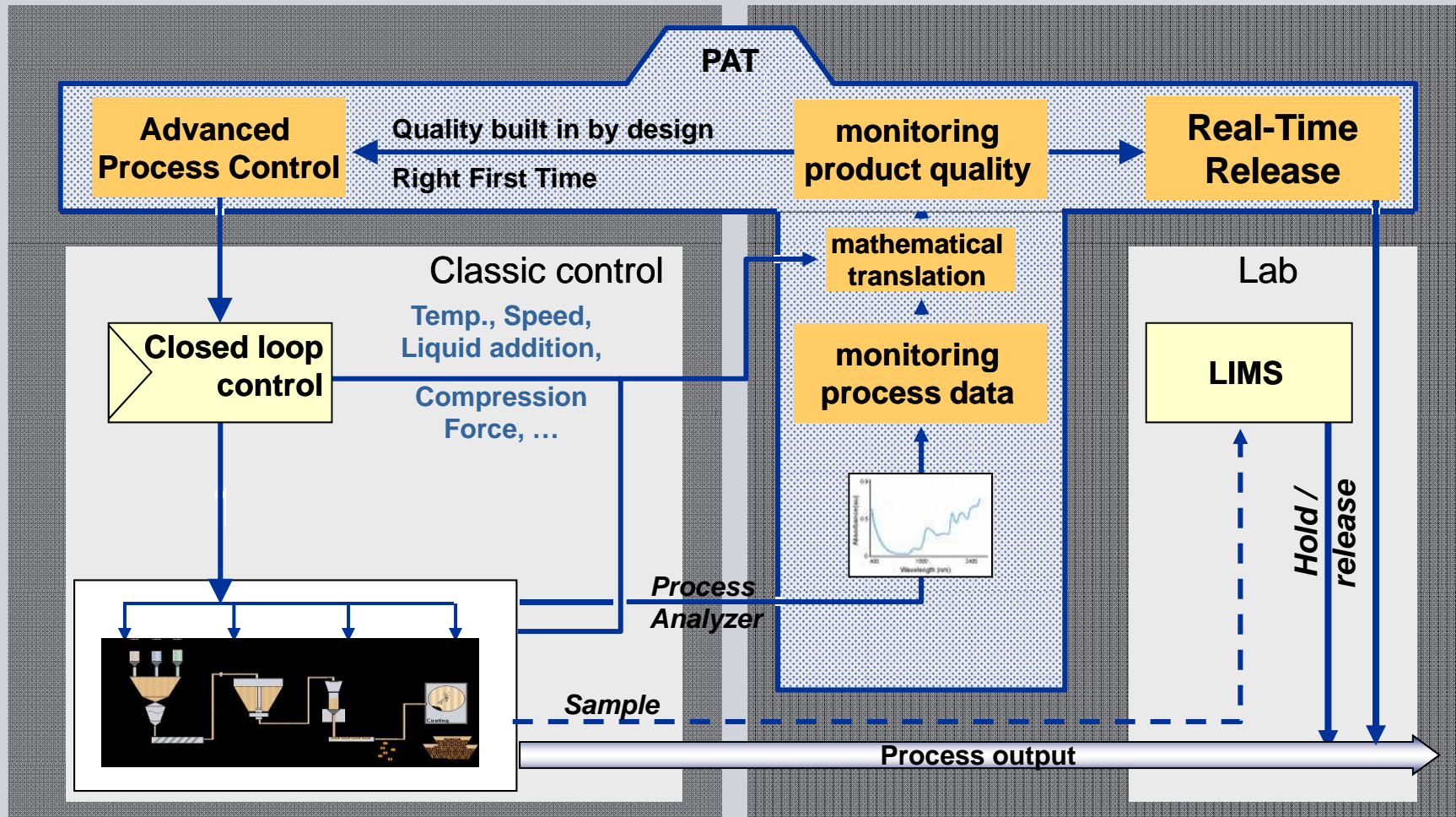
Reduce risks by improving safety (early fault detection, less invasive work for operators, better process control...)

Roadmap to an Advanced Process Optimization System

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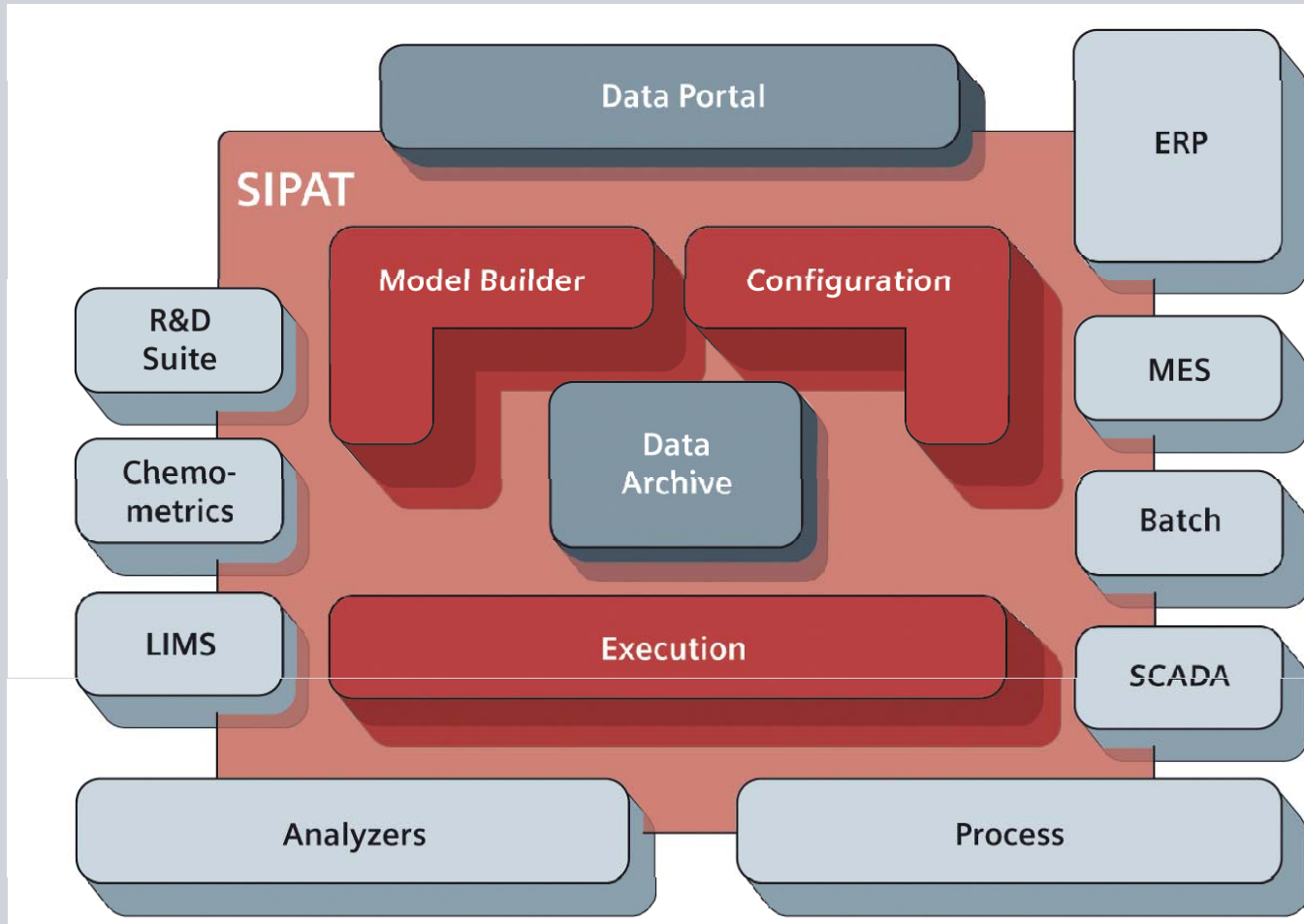


PAT Basics – Holistic Approach



PAT Architecture

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Cross-Functional Team and Network

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Demand
(Customer)



Raman Spectroscopy
NIR / MIR
Fluorescence
...

Team Lead

Supply
(Cross-Functional Team)

Project
Expert Team

Process, Production,
Analysis Experts
Internal and external

Integrator

System Design,
Development, IT

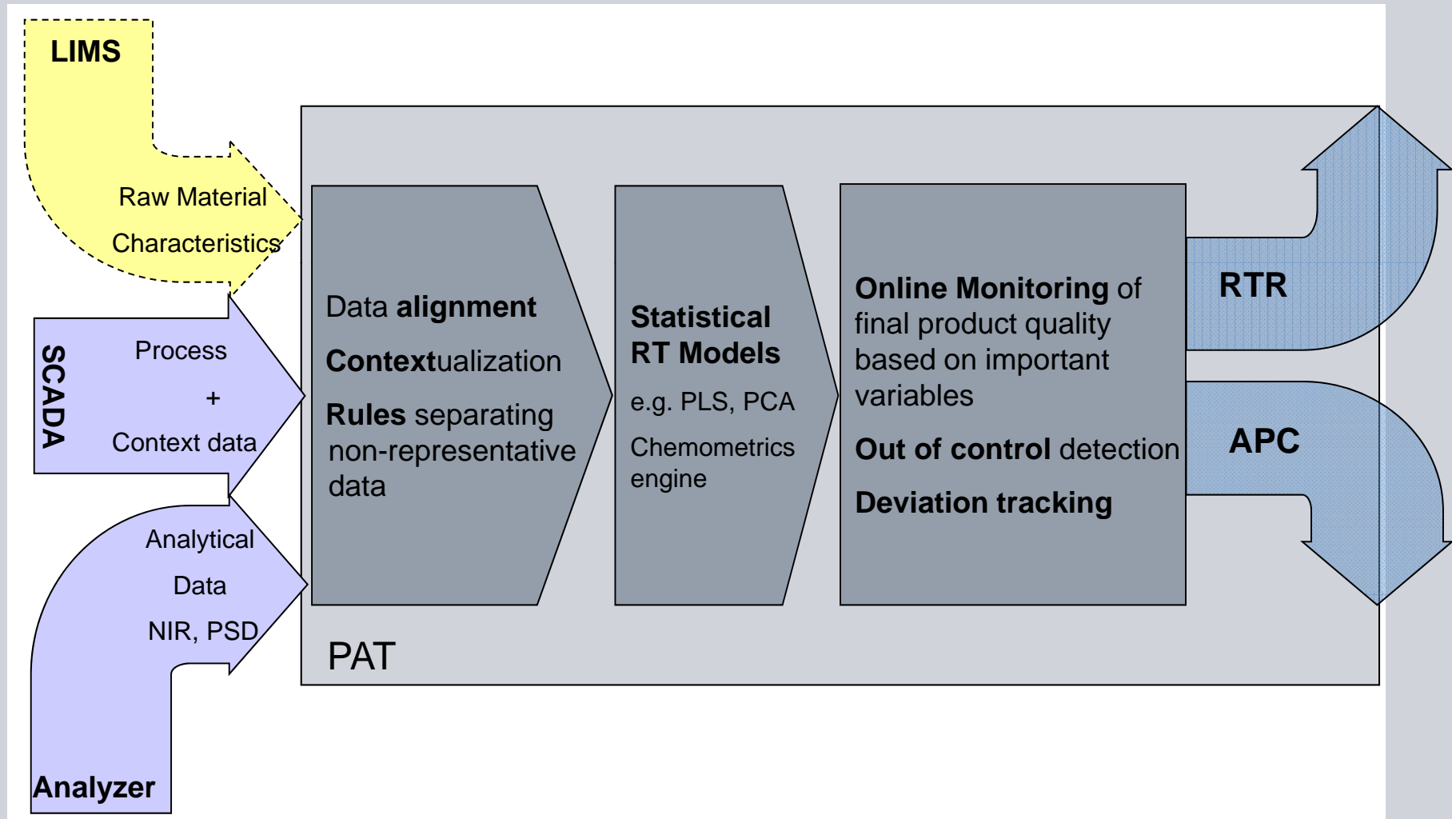
Suppliers

Automation , Device,
Analyzer Supplier

Team lead coordinates activities within team and involves production, process, laboratory, analyzer and data analysis experts as required.

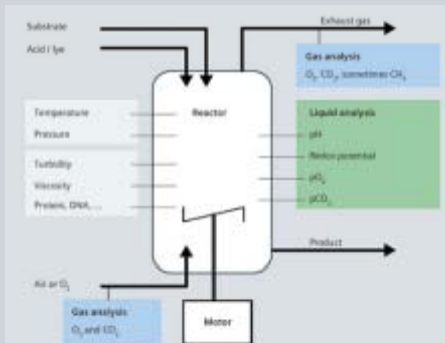
PAT Data Flow principle: focus on-line data acquisition and processing

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Example: E.coli producing recombinant protein – Modeling and Monitoring

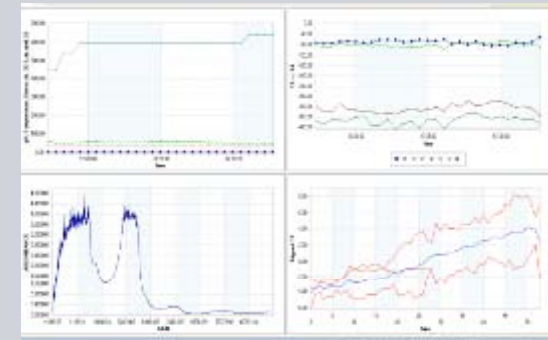
1. Bioprocess



2. Choice of sensors



3. Data capturing

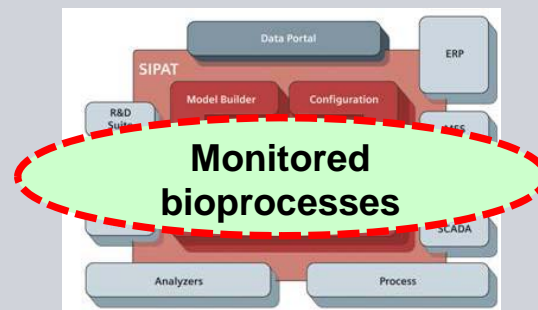
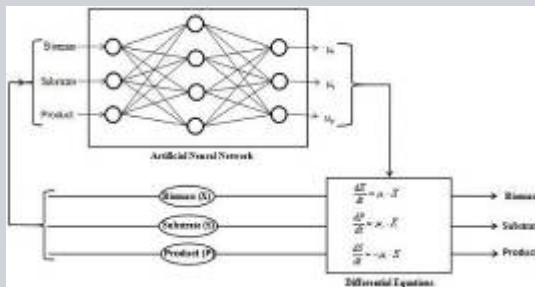


4. Control Variables selection

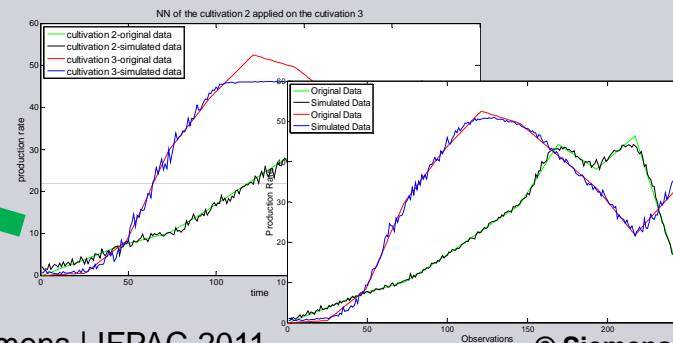
| Variables | |
|-------------|----------|
| Temperature | Biomass |
| qP | O2 |
| Gen Dosage | CO2 |
| Cell Count | Inducer |
| Product | Base |
| time | Capacity |

7. Generalization or Refinement for similar bioprocesses

6. Statistical and numerical solutions



5. Statistical modeling



Slide 11

BSK4

variable names change to understandable

Barbara Spangl-Kavsek, 1/14/2011

Data organization and analysis

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File formats

Merging of data streams

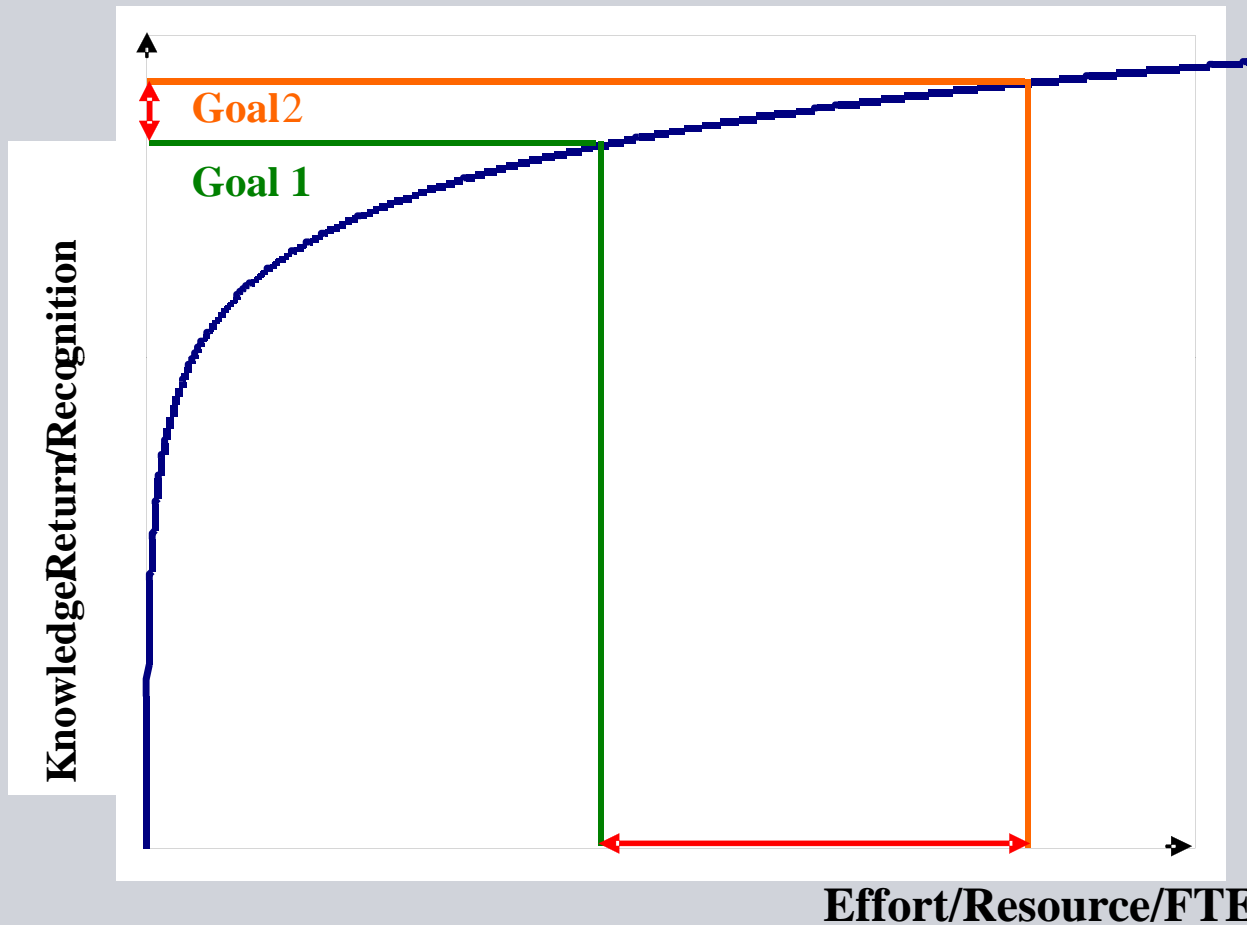
Analysis

- Preprocessing and data scaling
- Quantitative or qualitative analysis or both?
- Methodology: PLS, PCA, neural networks?

Model update – continuous learning, automatic or manual updates?

Setting Clear Project Goals & Objectives

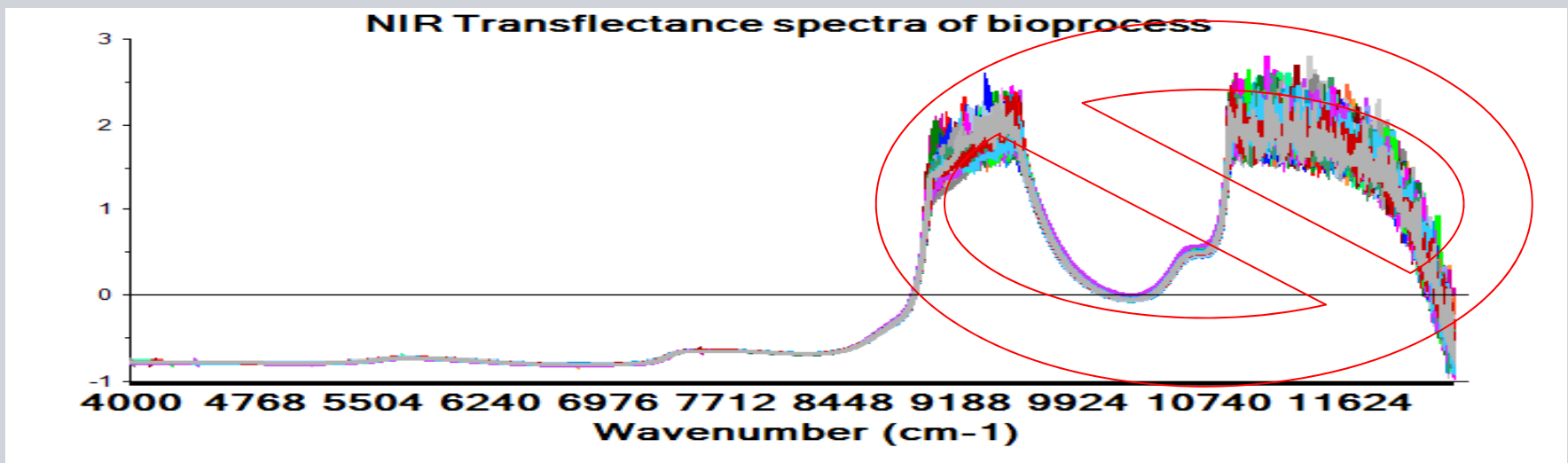
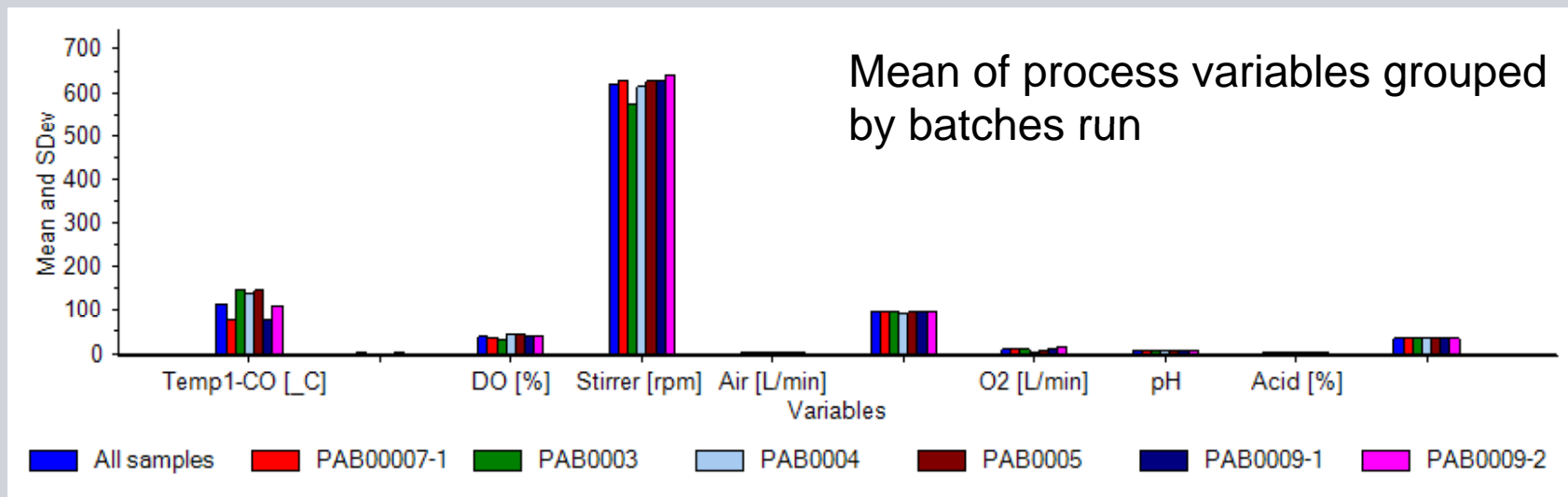
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Is the goal having a measurement that provides process information; or is it knowing everything about it and having the most expressive chemometric model and PAT tools to carry out the measurement?

Data analysis – begins with visualization

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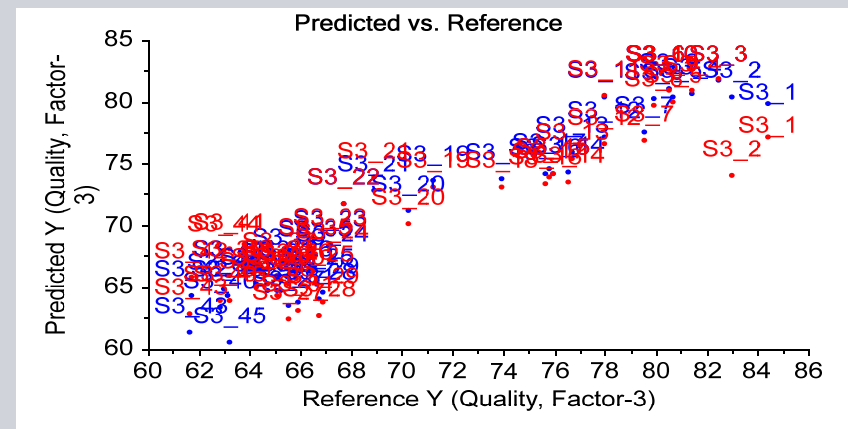
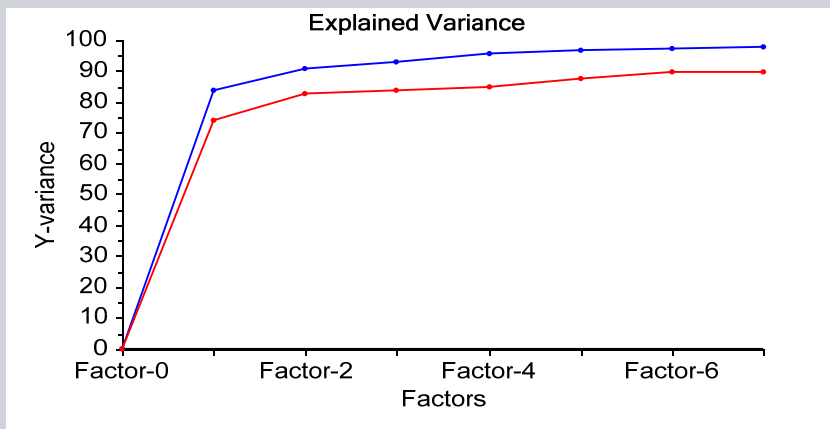
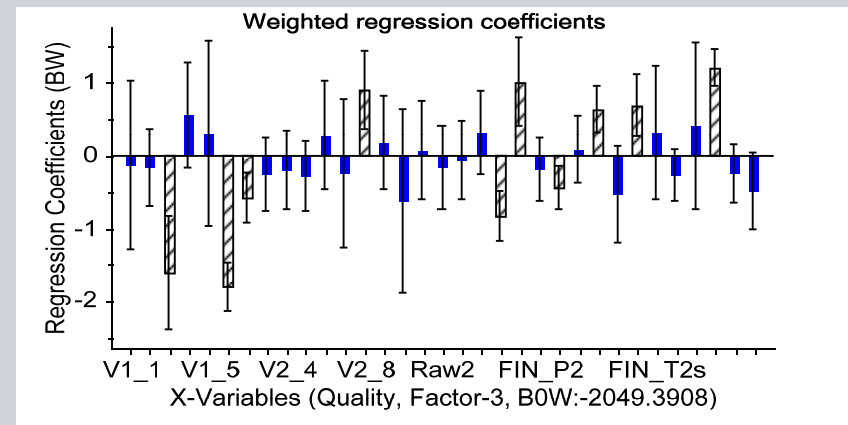
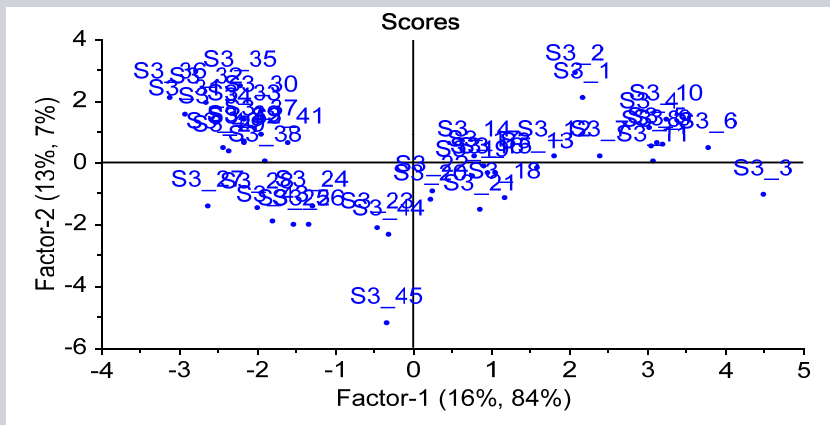


Data analysis

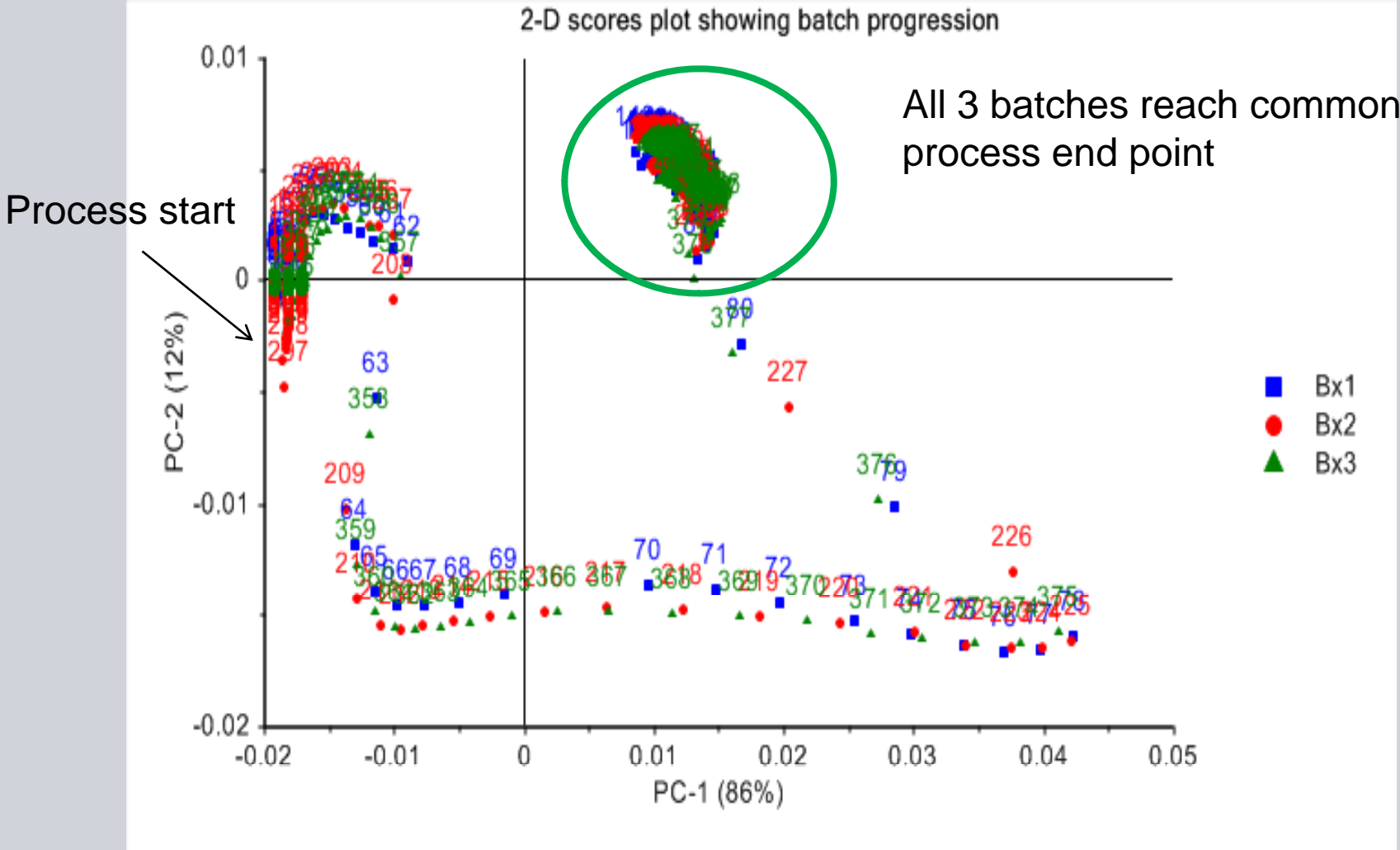
- Determine if data transformations (scaling, derivatives, scatter corrections) are needed to bring out signal from data and put variables on same scale
- Qualitative analysis can be used to give a process signature
- If have a quality parameter, or reference values for critical parameters, then quantitative regression models can be developed
- In all cases, models must be validated against independent data

Regression modeling of quality

Develop PLS regression model for product quality from 33 process parameters measured in chemical process; can use the model information to discern which variables are important in predicting quality



Qualitative analysis of data to show batch consistency of 3 batches?



Monitoring process with models: quantitative and quantitative

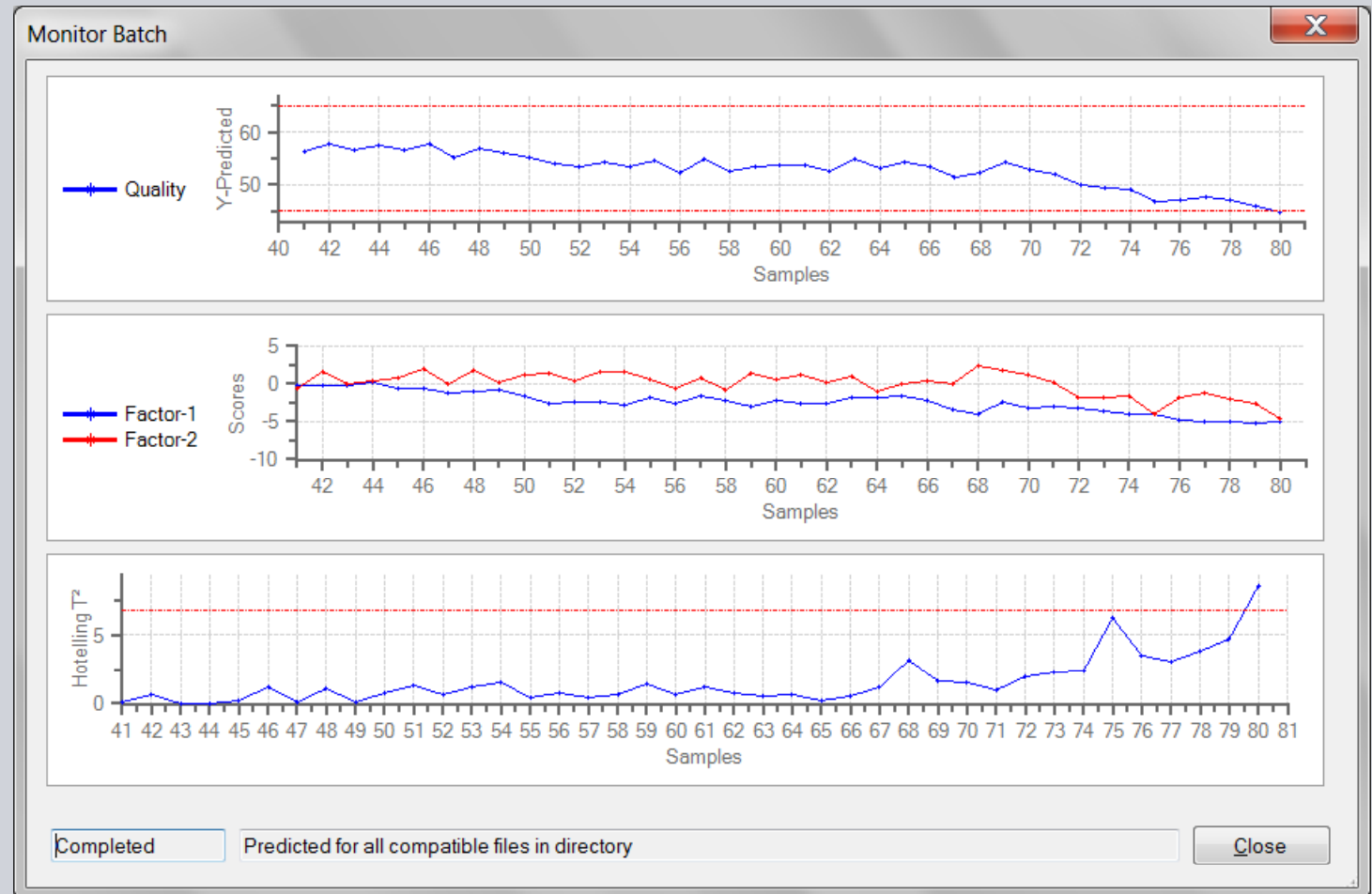
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PLS regression
for measuring
quality

PCA scores

statistical limit
at 95%
confidence



Advanced Process Optimization System

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System and Infrastructure

- Hard Elements (Devices, Analyzers, MES, LIMS, SCADA, ...)
- Soft Elements (Cross-functional team and network, internal and external)

Process

Measurement system

Models

Control Strategies

→ All together enable Advanced Process Optimization.

Conclusions

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Collecting quality data is just one part of the application; success is related to the knowledge gained about the process, and not to the volume of data generated

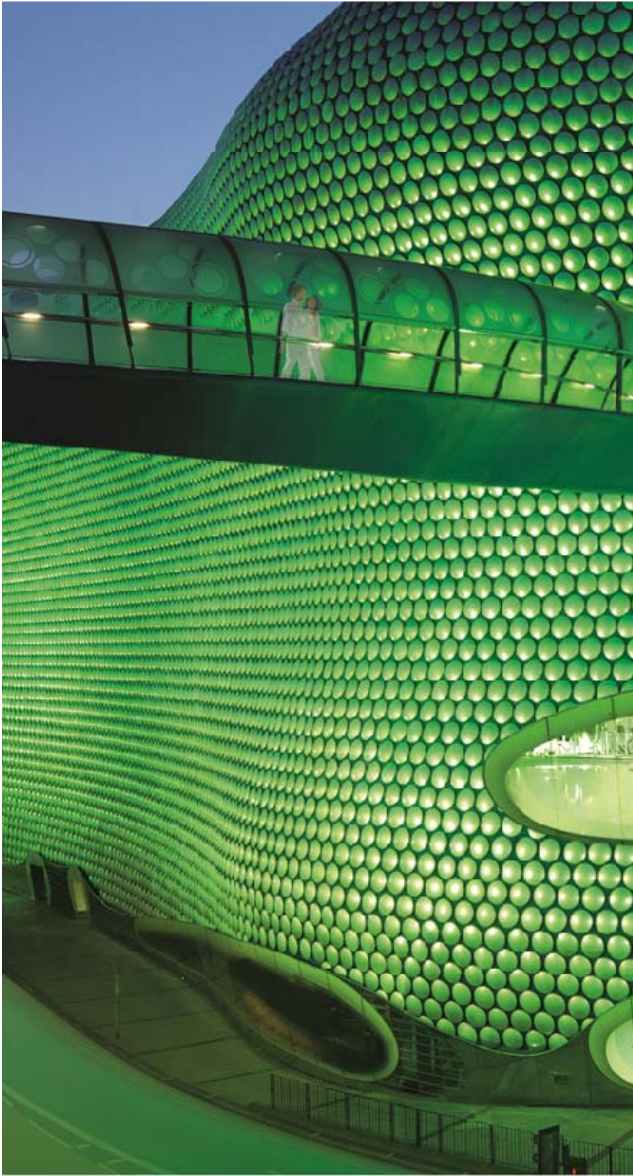
Provide infrastructure to handle the data as well as the tools to enable process optimization

Also need:

- Work in cooperation with the process owners
- Have buy-in and support from end-users
- Have good relationship with suppliers
- Collect the data to meet the control objectives
- Explore data analysis options that can be integrated with control systems



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THANK YOU FOR YOUR ATTENTION

ANY QUESTIONS?

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