PERCEPTIVE ENGINEERING LTD

PharmaMV
PAT, Advanced Control and Optimization Platform

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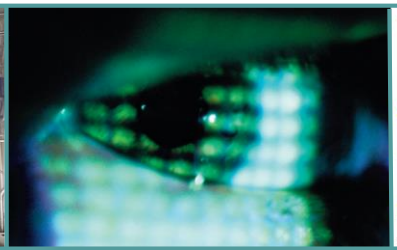
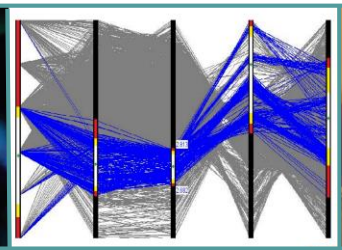
APMF 2015




Advanced Process Modelling Forum
Agenda

- Introduction to Perceptive Engineering
- PharmaMV Platform
- Perceptive Capabilities
- Look ahead to use of PharmaMV & gCRYSTAL models

Perceptive Engineering
Company

- **Spin-out 2003 Manchester University**
  - Department of Advanced Control
- **Engineers practical APC experience**
  - Average 8 years practical experience
  - Principal Team Leaders >15 years experience
- **Offices in UK and Singapore**
- **Academic alliances**
  - Universities of Cambridge, Manchester, Newcastle, TU Delft, UCL
  - CMAC & ICES – Alliance of several academic and industrial partners in continuous crystallization
  - CPI – Centre for Process Innovation

Perceptive Engineering
Company

- **What We Do:**
  - Perceptive Engineering develop and use a software toolset combined with engineering consultancy to create systems that optimise industrial manufacturing processes.
  - Introduction of control and monitoring technologies and techniques into a commercial offering for most non oil and gas manufacturing sectors.
- **Our Approach to R&D**
  - Translation of academic research into market driven and robust industrial solutions.
  - Collaborative R&D leverages resources and skillsets from multiple parties, each deriving benefits, to meet their own distinctive needs.

Perceptive Engineering
Software Family

Off-line development, analysis, visualisation and assessment:
find out how capable your plant can be

On-line process improvement:
get the most from your process, all the time

Industry-specific enhanced toolsets:
designed to meet unique challenges

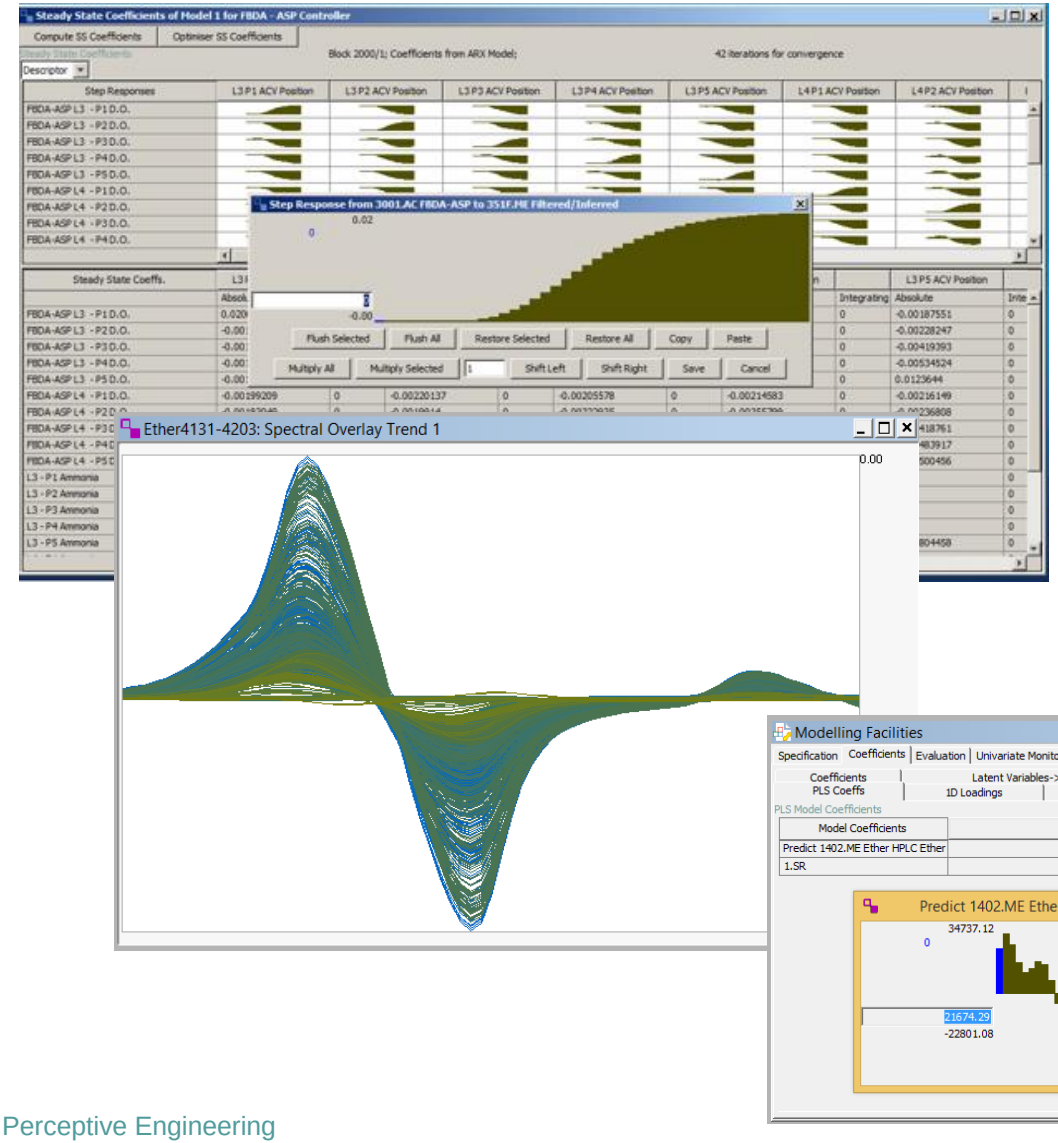
Philosophy

- **A software platform for Advanced Process Control in the Pharmaceutical Industry:**
- **Some of the challenges….**
  - Management of "Instrument and Data" Integrity
  - Capability to deal with Batch and Continuous Processes
  - Interconnectivity – Use of existing industrial standards.
  - Delivering Fault tolerant Monitoring, Control, Optimization.
  - Traceable User Actions and 21CFR Part 11 Compliance.
- **Blending the Pharmaceutical Scientist and Automation Engineering disciplines**

Manufacturing Intelligence
Software for Real Time Analysis and Control

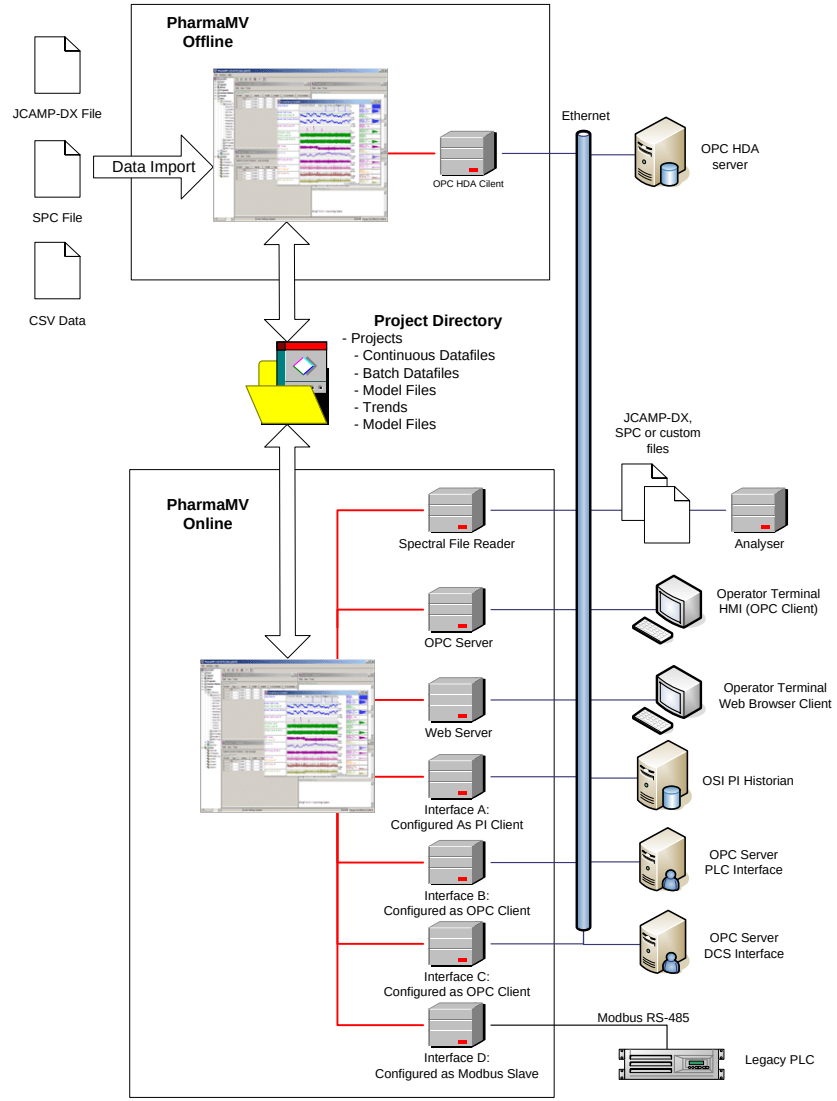
- Data Import/Export
- Data Quality Monitoring
- Data Analysis
- SPC Monitoring
- Multivariate Modelling
- Multivariate Process Monitoring
- Multivariate MPC
- Continuous / Batch Optimisation

Before we go any further…
Setting the scene on the word "Model"

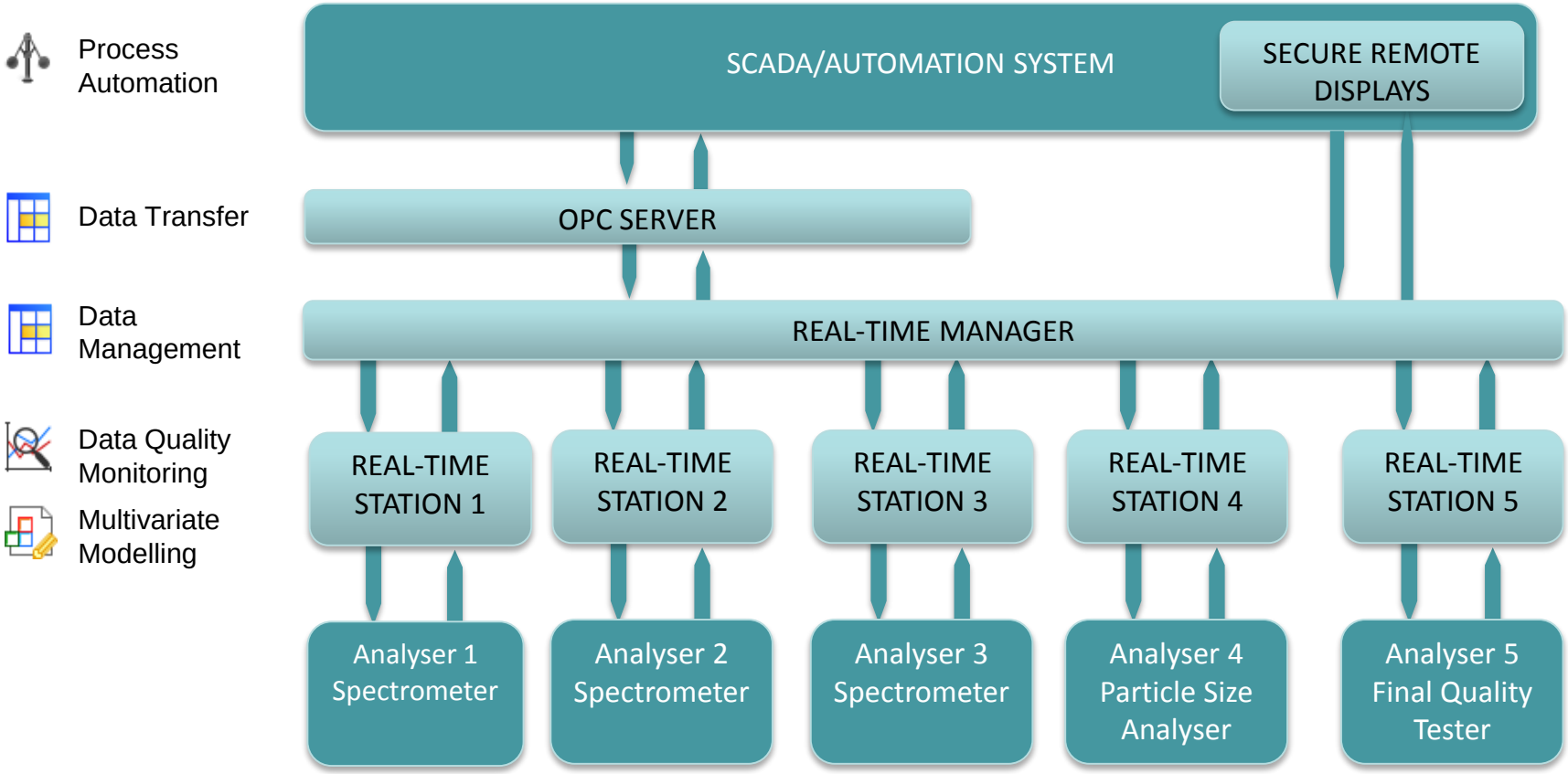


- **Stochastic Models for**
  - Dynamic Control
  - Predictions
  - Calibration etc.
- **Created from**
  - Designed Plant Tests
  - Historical Process Data

PharmaMV Platform Architecture
Real-Time Connectivity

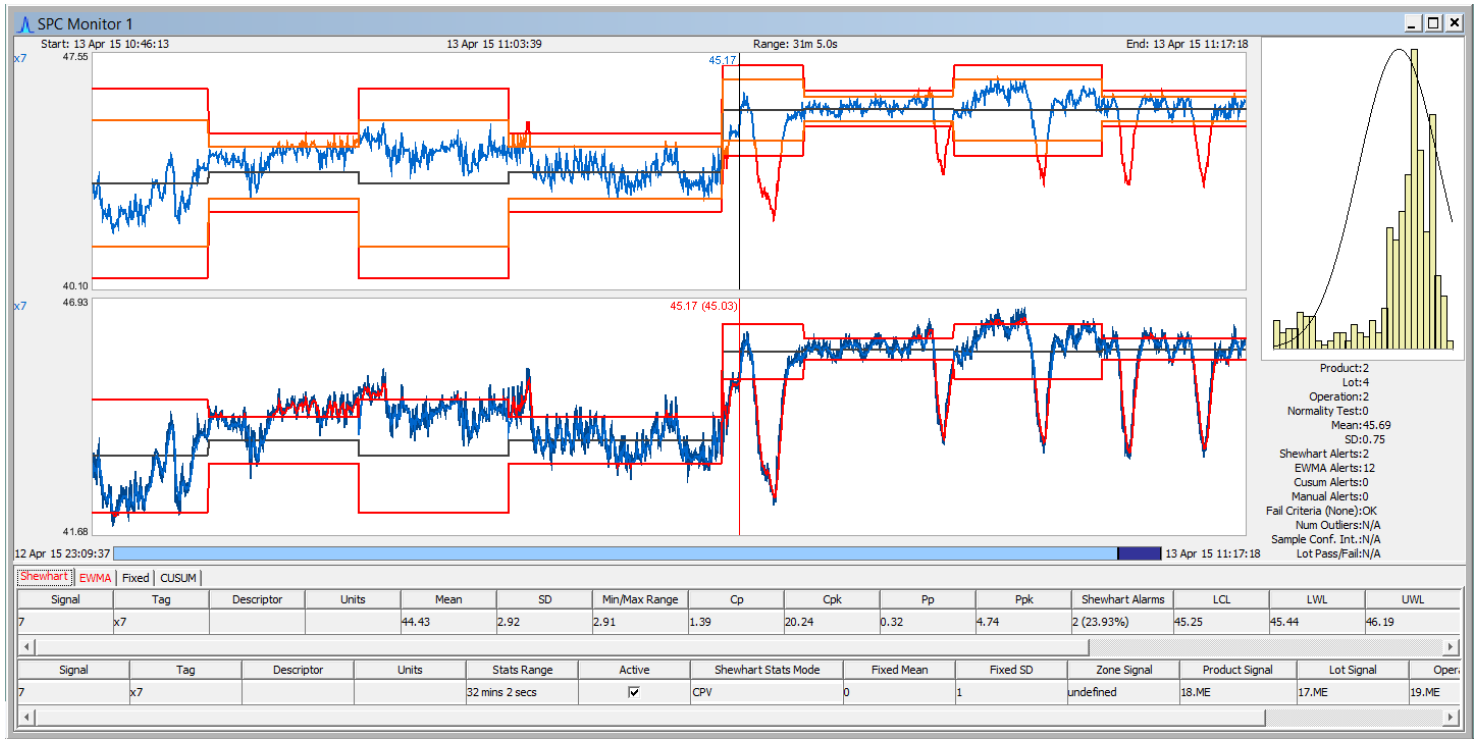


PharmaMV Platform
Real-Time Manager and Spectral Data

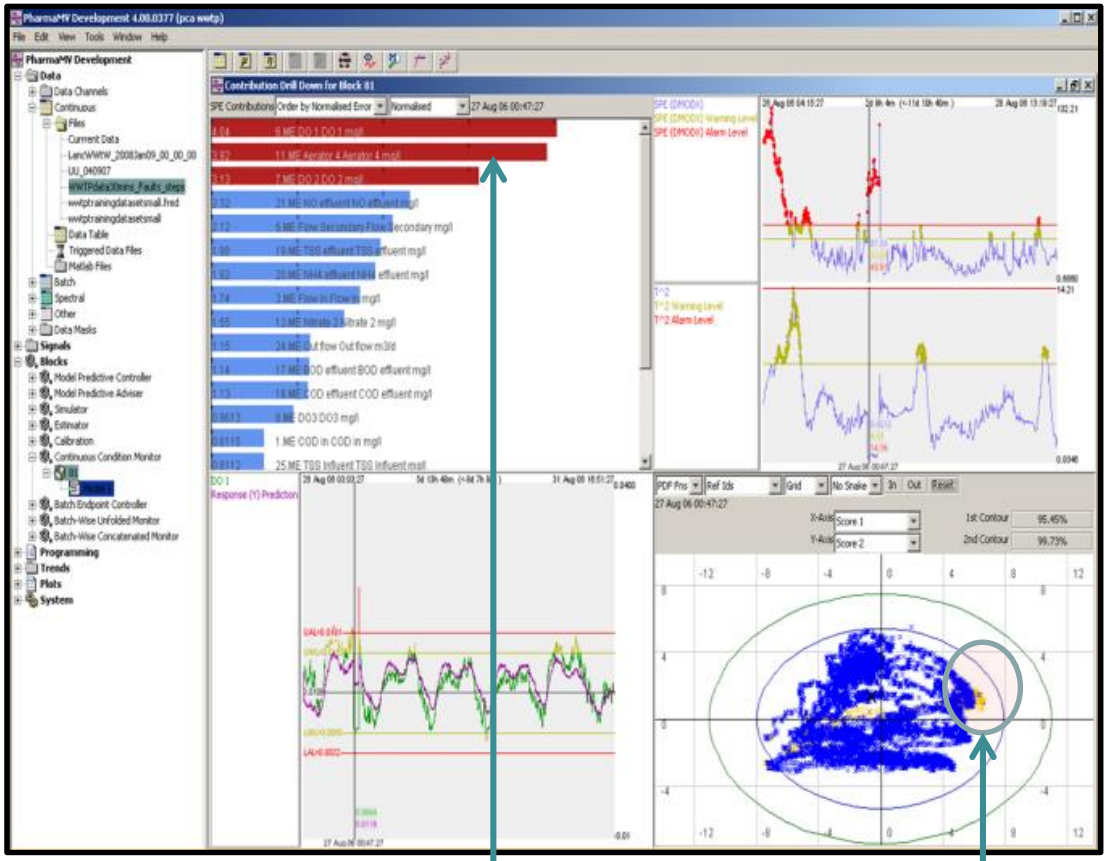


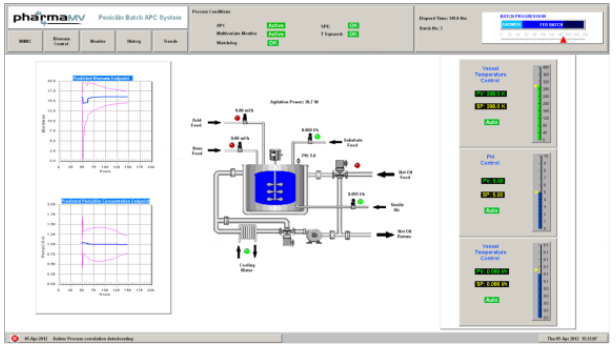
Univariate Process Monitoring
Continuous Process Verification

- **Real-time abnormal operation detection**
  - Statistical rules
  - Control Limits update based on Product / Lot / Operation of process



Multivariate Process Monitoring
Continuous Process Verification



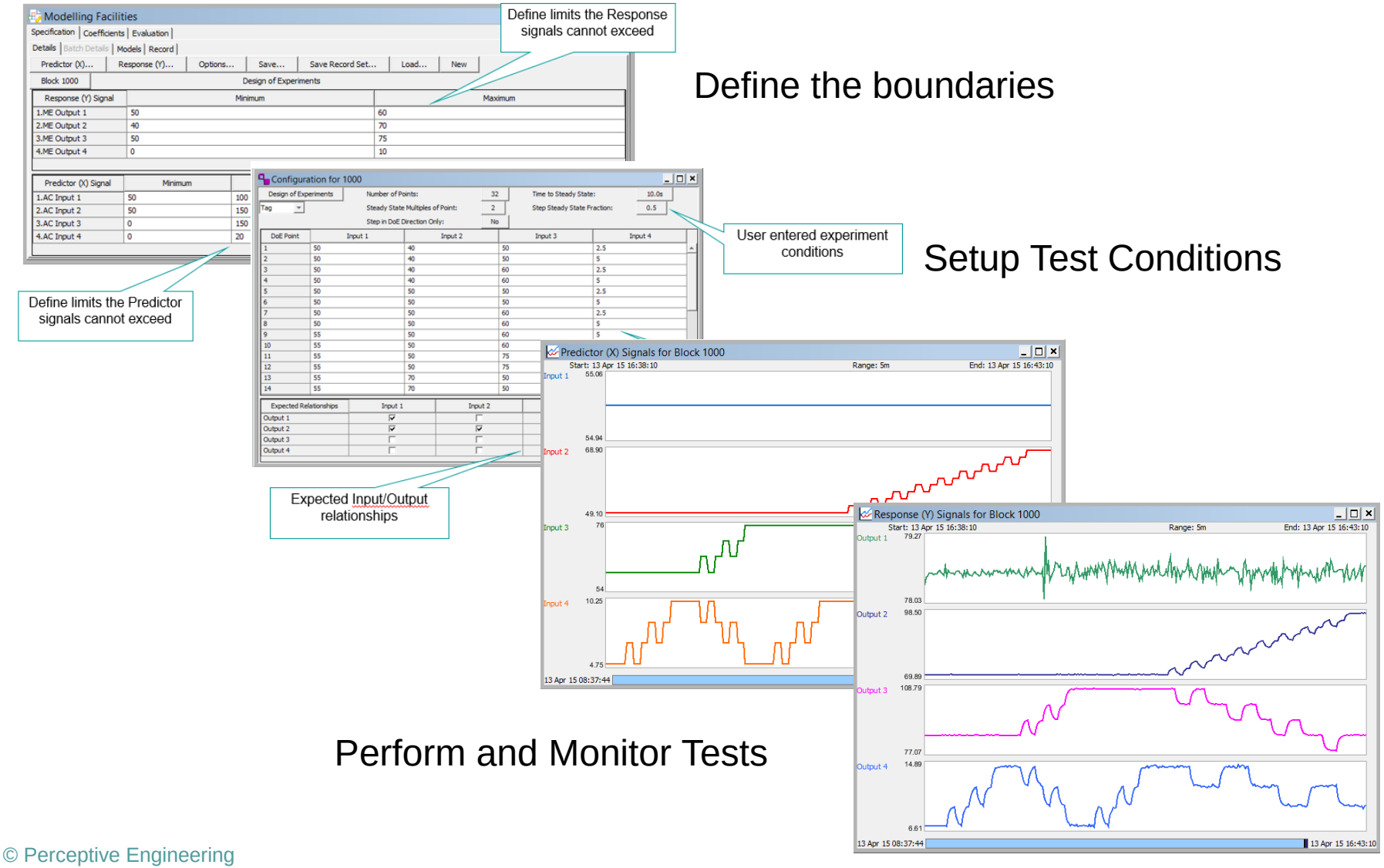


Guided Analysis for both Operator and Engineer.

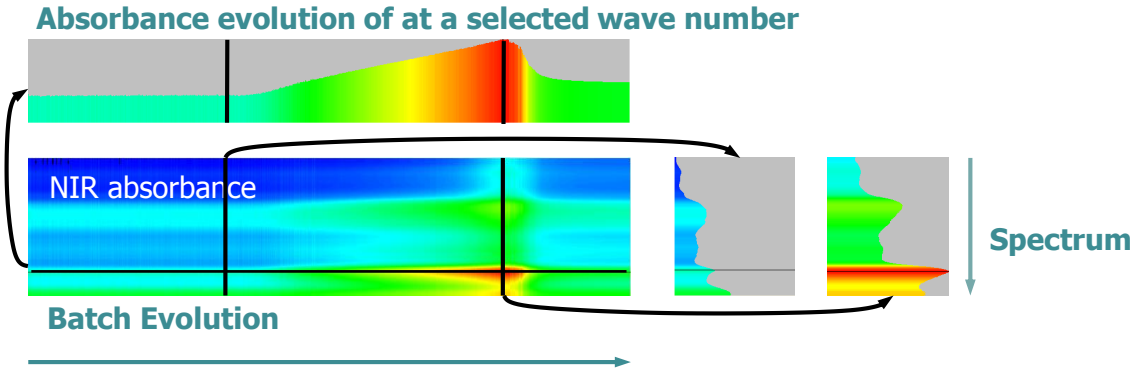
Diagnose Process Fault

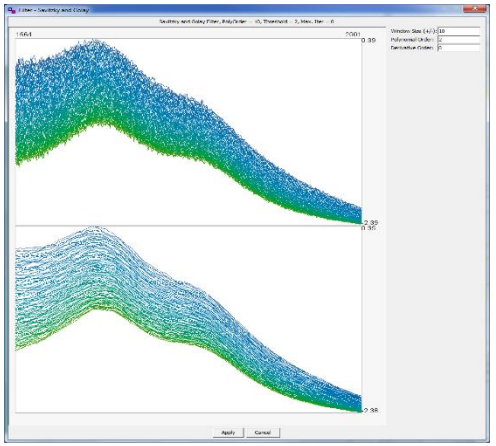
Process Abnormal Operation

Automated Plant Testing
Design of Experiments / Process Response Testing

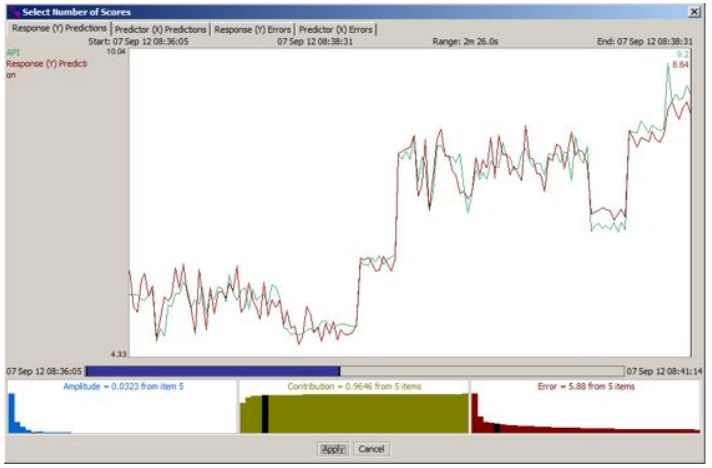


Process Analytical Technology (PAT)
Data Processing / Analysis and Calibration Models



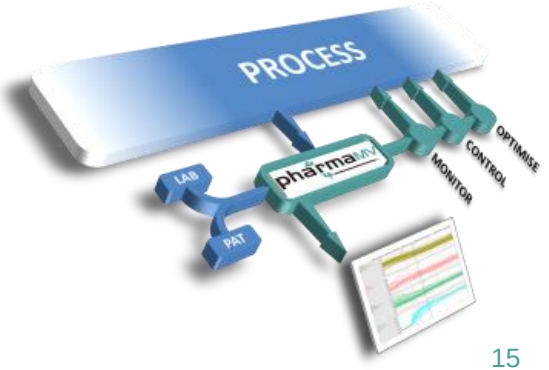


- **Using Process Analytical Technology (PAT) in control offers great possibilities**
  - Using modern PAT devices capable of 1-2 second or sub-second measurement rates, real-time control based on PAT measurement is a reality
  - Sensor calibration models can give real time inference of product property



PharmaMV Platform
Pharma and CPG Applications

- **APC for API Manufacture**
  - Crystallisation
  - Continuous and Batch
  - Solvent Extraction
- **APC for Solid Dose Form**
  - Blending, Granulation, Drying, Coating and Tableting
- **APC for Fermentation**
  - Run to Run Optimisation
- **APC for Drying**
  - Nutritional Powders



PharmaMV Platform
Batch Crystallisation Concentration Prediction

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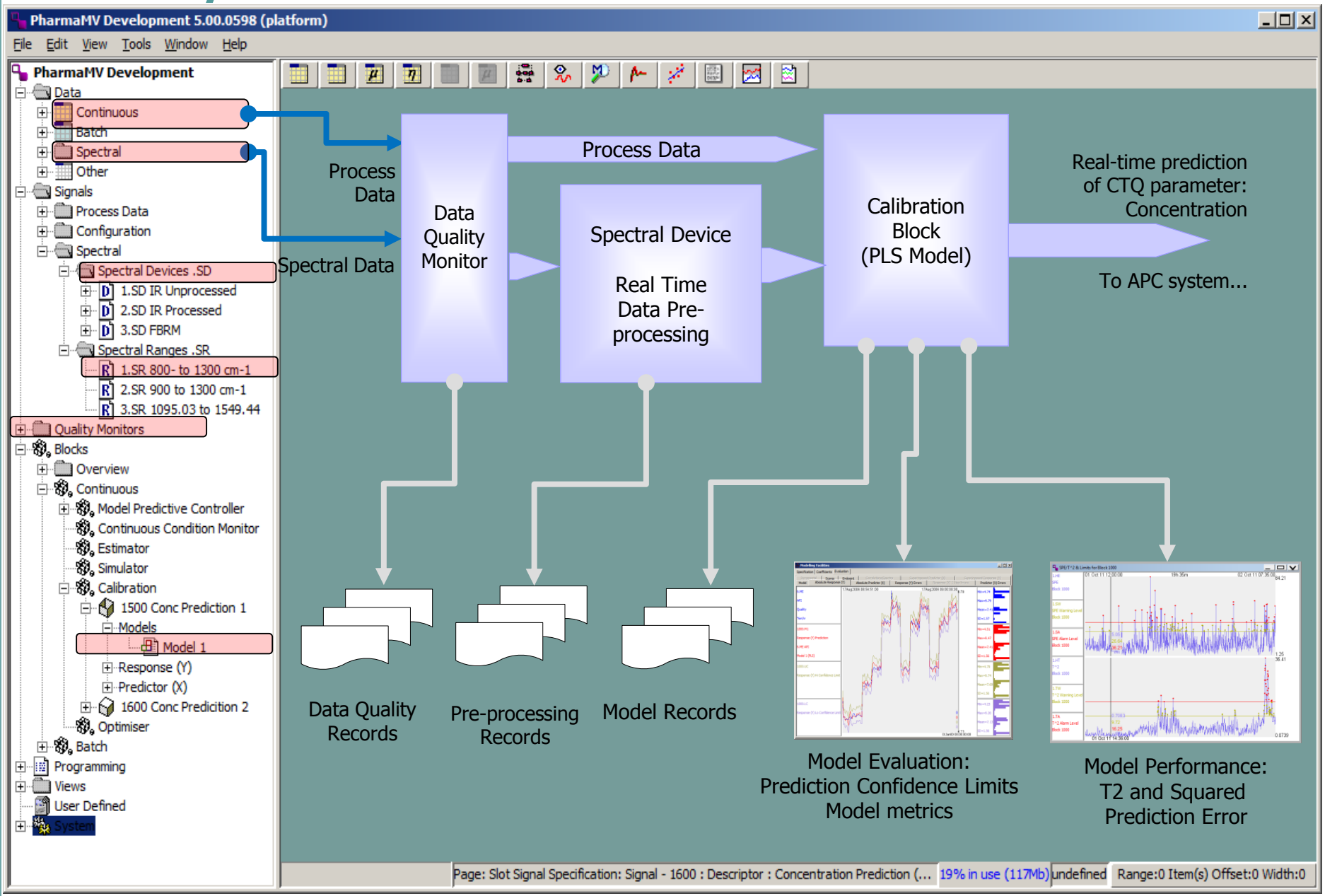

PharmaMV Platform
Batch Crystallisation APC System

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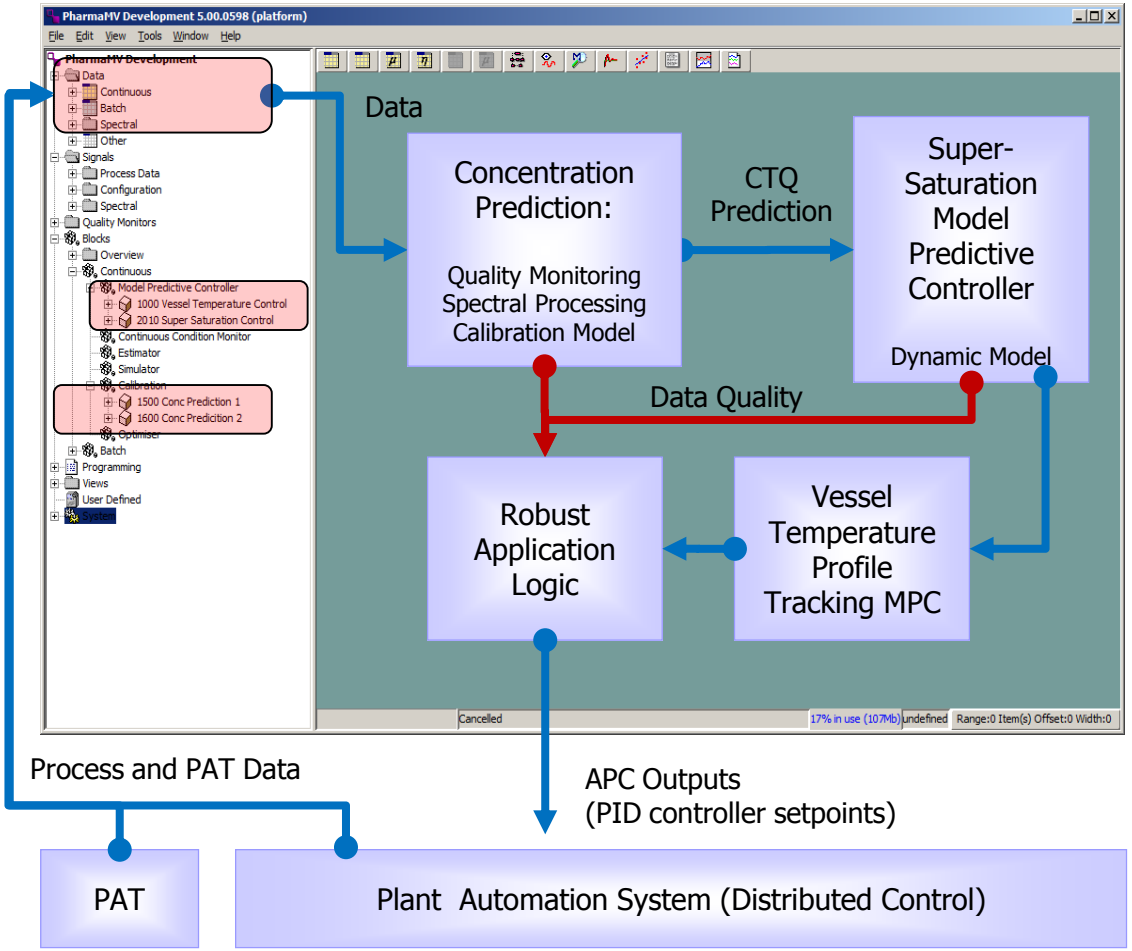
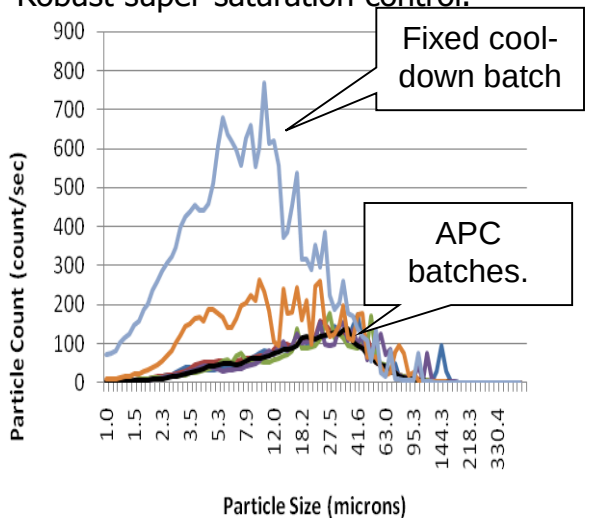
Batch Crystallization Real-Time APC System



An integrated platform for improved cool-down crystallization

- Automated Meta-stable zone identification for product development and scale-up.
- Validated Real-time concentration prediction.
- Robust super-saturation control.

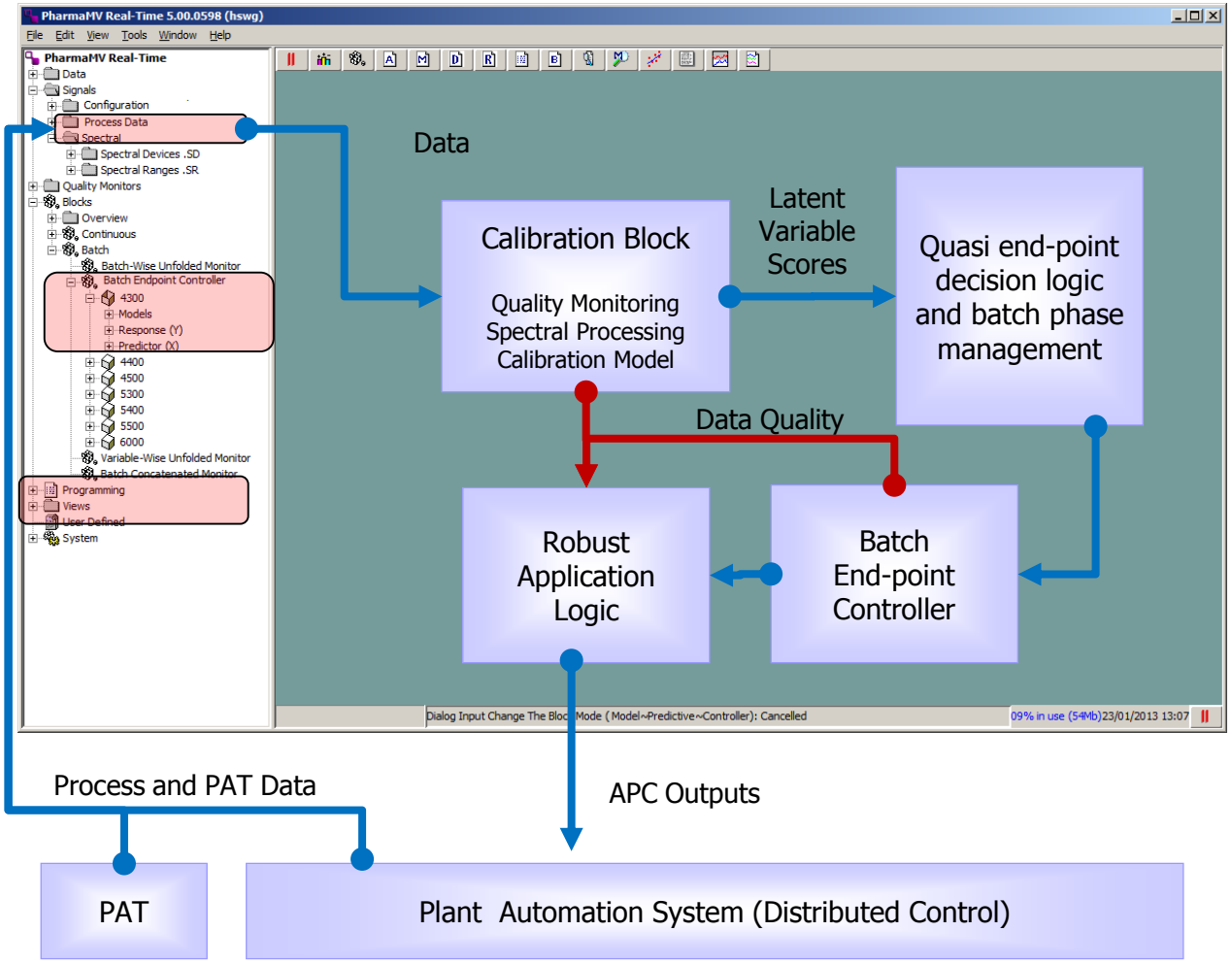


High Shear Wet Granulation (HSWG)

- **Monitoring and/or control of High-Shear Wet Granulation**
  - NIR PAT modelled to generate latent variable score trajectories in real-time
  - Batch unfolded techniques to control and/or monitor the process based on these trajectories
- **Objectives:**
  - Control the process to a "golden batch" trajectory
  - Respond to variations in raw material and other factors

PharmaMV Platform
High Shear Wet Granulation (HSWG)

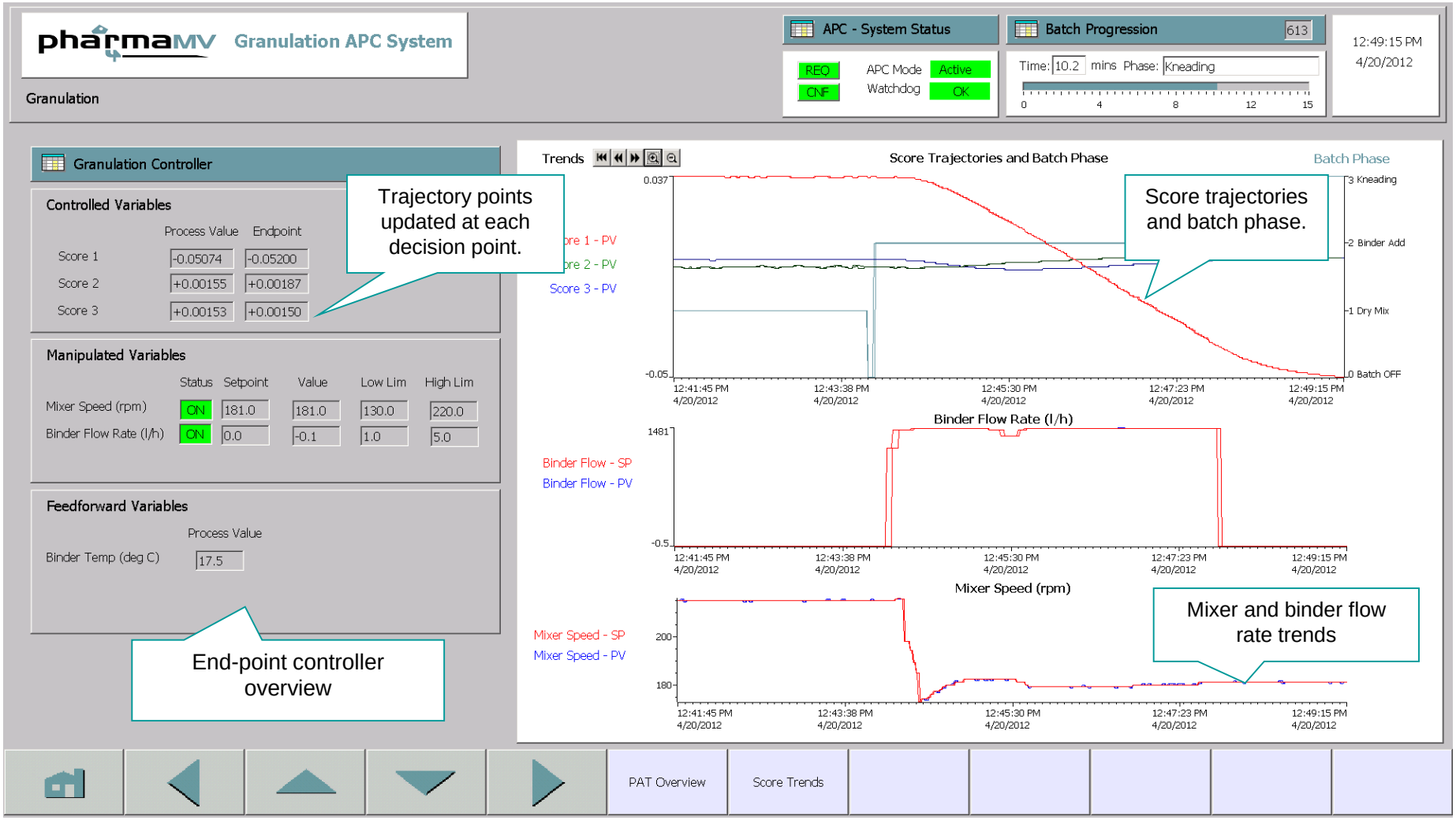
HSWG Real-Time APC System



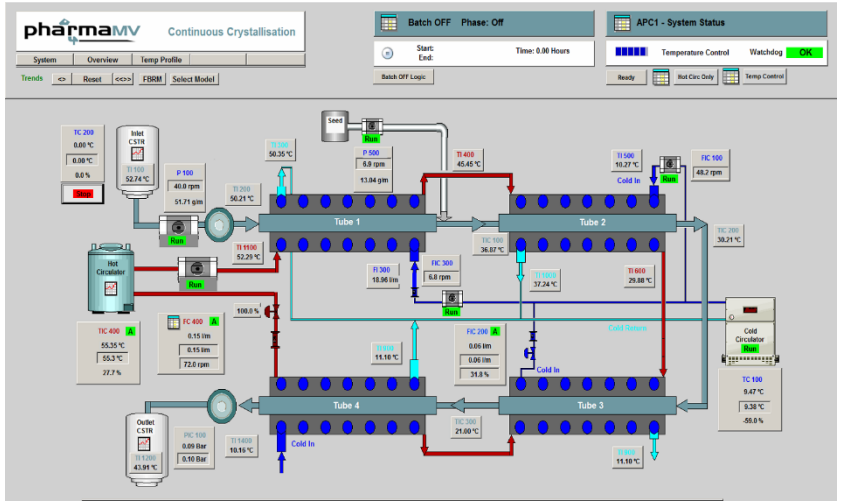
An integrated platform for HSWG control and monitoring

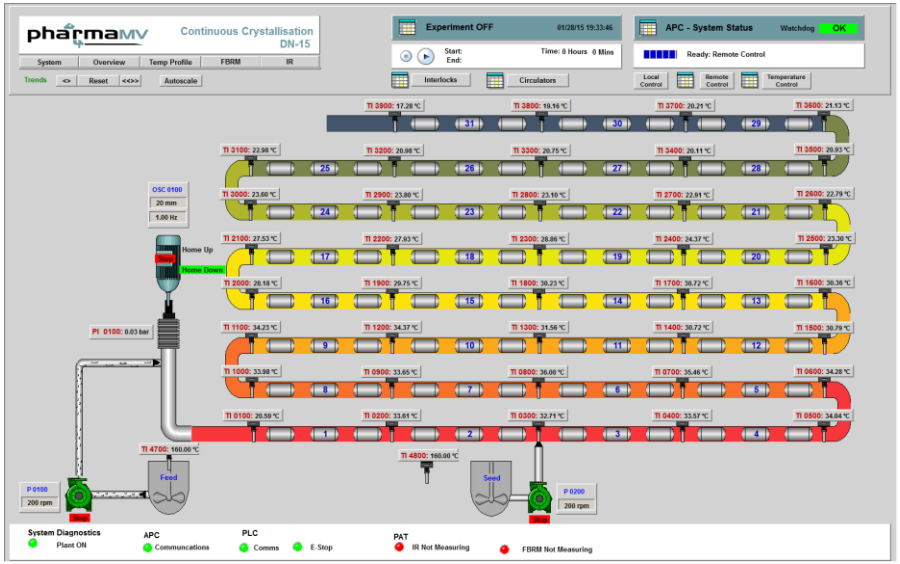
- The latent variable scores describe the key features of the NIR spectrum.
- A batch-end point controller is used to adjust the batch trajectory at key decision points. The controller automatically switches models based on the batch phase.

PharmaMV Platform
High Shear Wet Granulation (HSWG) for Operators

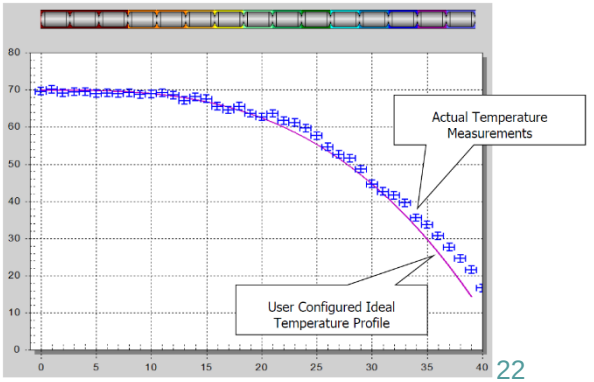


Continuous Crystallisation
Continuous Oscillatory Baffle Reactor



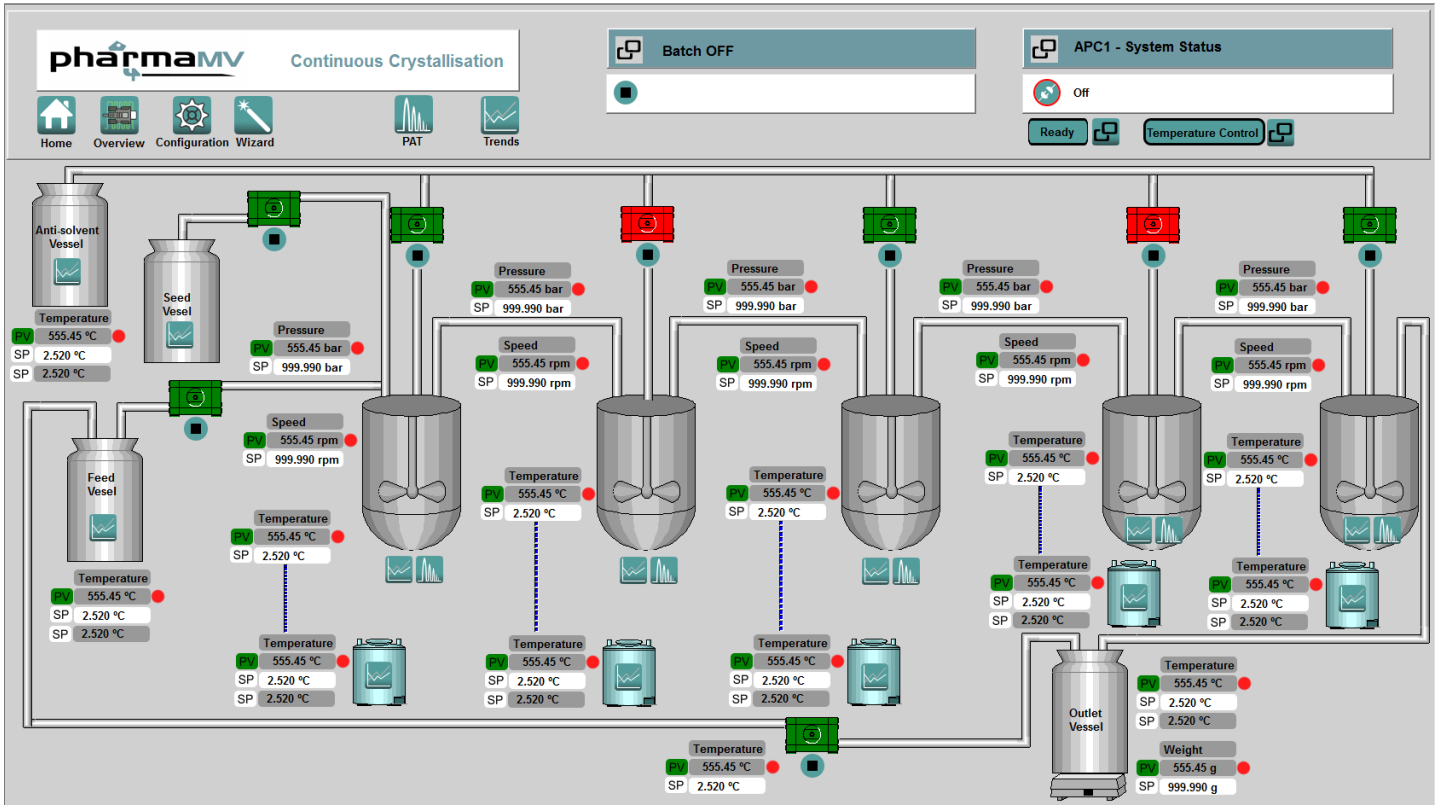


- **Main features:**
  - Data acquisition, fail-safe automation interface and operator advisory display for
    - Thermocouples
    - Oscillator
    - Pumps
  - Data acquisition and interface to PAT devices including
    - FBRM
    - FTIR
    - Raman
    - React IR
  - Vessel Temperature Control display



PharmaMV Platform
Continuous Crystallisation (CSTR/MSMPR/Anti Solvent)

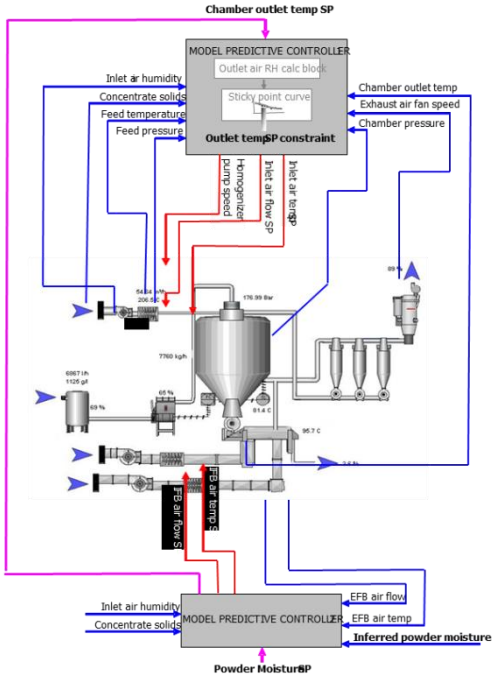
- **PharmaMV Platform**
  - Flexible design to allow unit to be operated in different modes dependant on requirements

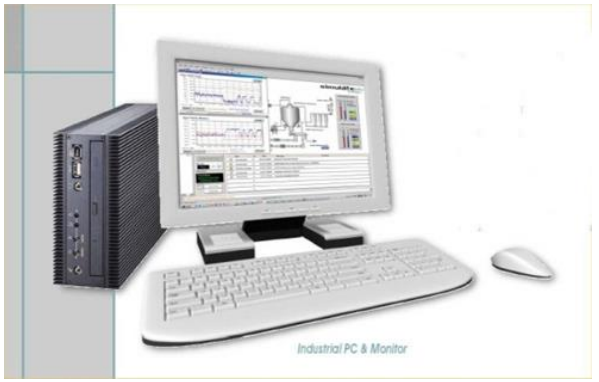


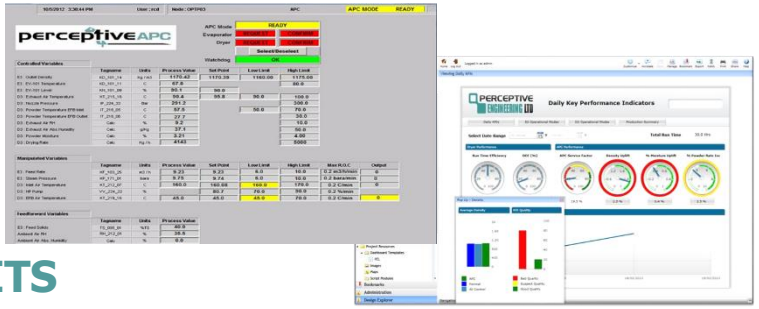
Nutritional Powders Solution
APC & Optimisation

- Data Quality Monitor
- KPIs
- Thermodynamic Calculations
- Soft sensors
- Evaporator/ Dryer Start-up
- APC & Optimisation

REAL TIME



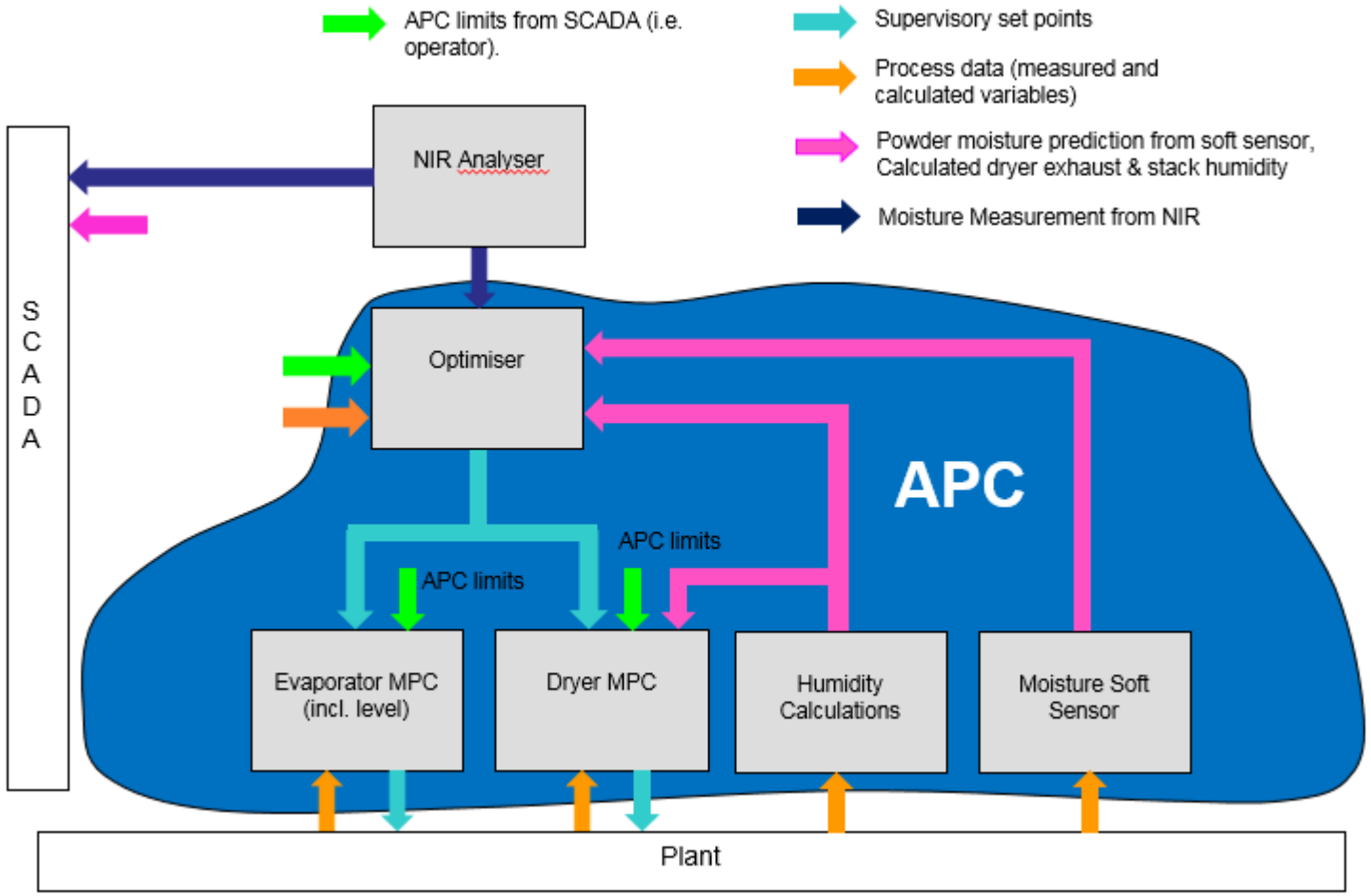




- **BENEFITS**
  - Stabilise process & reduce variability
  - Improve quality compliance
  - Increase yield and capacity
  - Reduce specific energy consumption

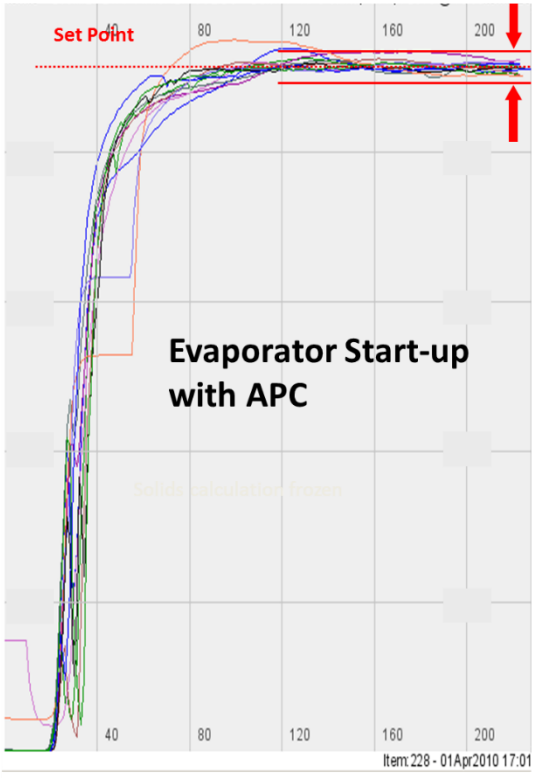
Nutritional Powders Solution
APC & Optimisation

- **The Foundation of our Solution**

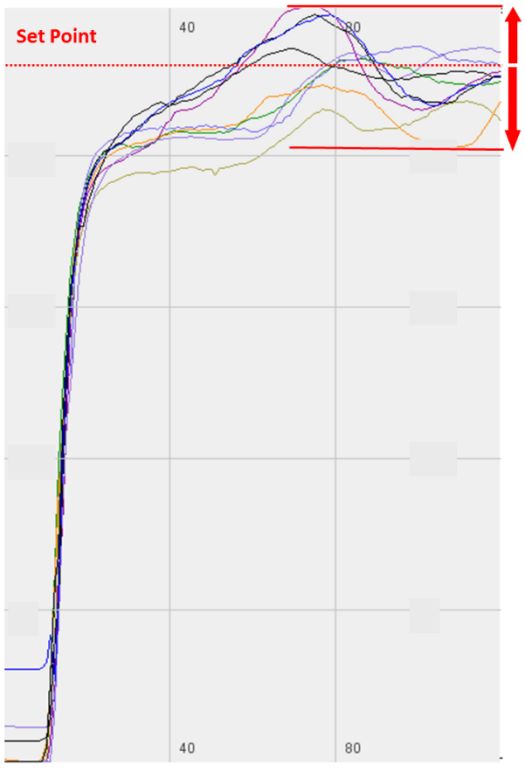


Nutritional Powders Solution
Evaporator and Dryer Start-up

Water → Product start-up with APC



Multiples of 16s (1 hour span)



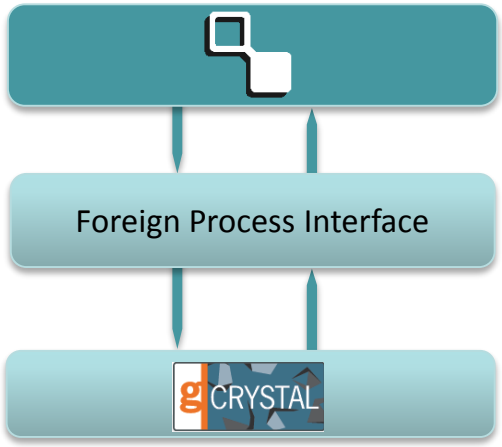
Multiples of 32s (1 hour span)

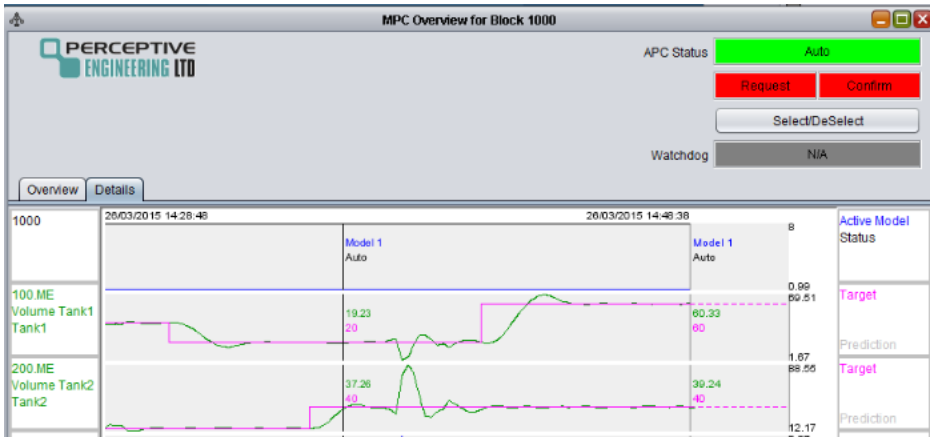
Look ahead to new approaches

- **Process Monitoring / Control / Simulation and Optimisation**
  - Current Models are data driven
    - Involves plant testing
    - Cost of raw materials
    - Availability of plant for testing
    - Existing historical data could be in a narrow band of operation
  - Could
    - Plant testing be performed on a mechanistic model?
    - A process be monitored / controlled directly via a mechanistic model?
    - Increase the use of multivariable control / monitoring at design time?
    - Process capability increase at design time?

PharmaMV with gCRYSTAL
Process Units

- **PharmaMV using gCRYSTAL as a process unit**
  - Process testing and advanced control design

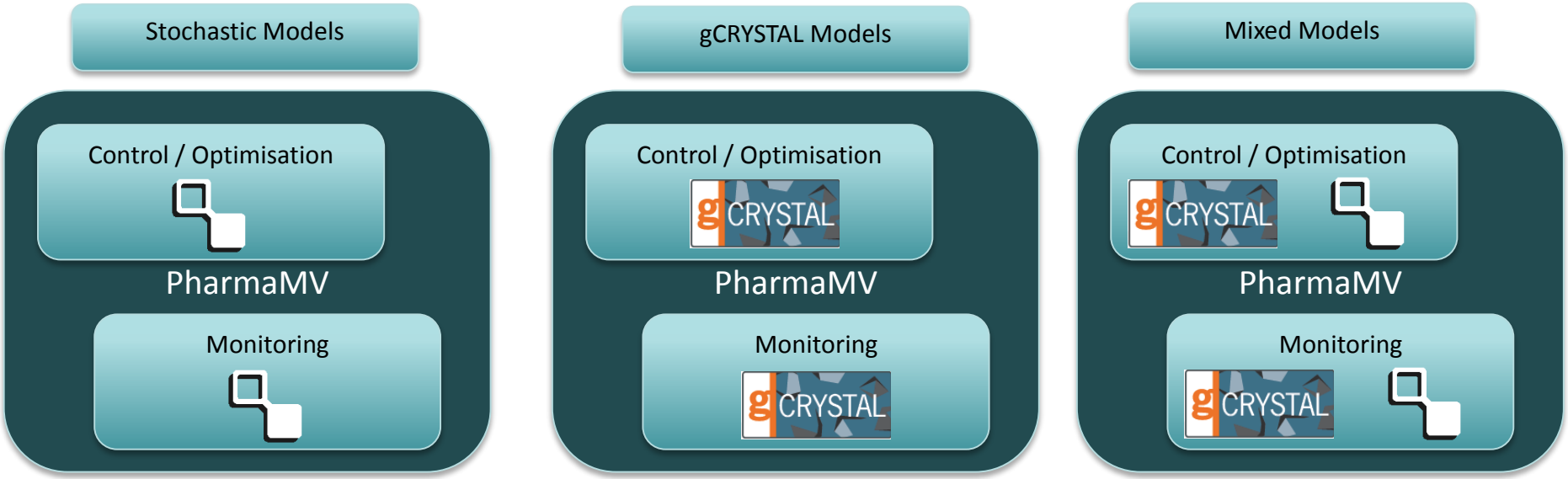




- **Potential Application & Benefits**
  - Selection of control parameters, initial process testing and model design on a model
  - Reduction on material required to build models
  - Reduction on time required on site, process availability
  - Reduced control/monitor commissioning time.

PharmaMV with gCRYSTAL
Mixed /Hybrid approach

- **Mixed / Hybrid approach to control and monitoring.**



- **Potential Application & Benefits**
  - Reduced or minimal process testing required
  - Models available for variables that may not have been possible before

Any Questions...
Just Ask!

Andy Mitchell
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