

Lean Model Management for Production Environments

Formulation 4.0

13 December 2018



Lean Model Management Overview

Perceptive Engineering

- About Us
- Process Agility: Challenges and Solutions
- Model Development, Validation
- Model Management
- Model Deployment - Optimised Manufacturing
- Summary, Q&A



Lean Model Management

Perceptive Engineering

Who

- Industrial Advanced Process Control
- 25 APC Engineers
- Offices in UK, Singapore, Ireland

Where

- Pharmaceutical
- Consumer Packaged Goods
- Environmental (Clean & Wastewater)

Academic / Innovation Alliances









- Universities of Cambridge, Manchester, Newcastle, Rutgers, UCL, Strathclyde, Leeds, Surrey
- Centre for Process Innovation (CPI), Centre for Continuous Manufacturing and Crystallisation (CMAC), Institute of Chemical and Engineering Sciences (ICES Singapore), Research Centre Pharmaceutical Engineering (RCPE), Synthesis and Solid-state Pharmaceutical Centre (SSPC)
- Industrial partnership with Siemens and GEA



Lean Model Management

PerceptiveAPC Software Platform



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

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Process Agility: Challenges

Spectrum

- Bulk powder production: 1 product equates to >90% of annual tonnage
- High-value manufacturing: multiple grades or recipes in 1 day
- **Need:** re-task production assets as quickly as possible (just-in-time manufacturing)

Distributed Data

- Process and Quality data generated per product, per variant, per process line, per plant
- No global historian?

How To

- Manage the complexity of multiple recipes, multiple raw materials, multiple CQAs
- Define impact of multiple variables from time-separated production runs
- Keep process models up-to-date
- Avoid compromise:
 - Why can't we have efficiency, energy saving and waste reduction at the same time?

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Process Agility: Solutions

Model what you're making, not just what you're making it with

- Statistical modelling lets us predict end quality properties
- The prediction is another feedback signal into control of the process
- Digital model of the process: what to change, when, by how much, ahead of time

Cloud computing can bring people, data and models together

- Secure data storage
- Ease of access
- Appropriate model selection – a global MES

Context-driven machine learning keeps models updated

- Models updated as needed
- Context ensures models remain fit-for-purpose
- Machine-learning can learn the wrong thing (ever bought an Amazon suggestion?)



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Process Agility: Solutions

Pharmaceutical

- Traditionally batch: add everything, mix and react, test at the end
- PAT devices provide insight into batch development
- Model-based optimisation
 - batch endpoint prediction, batch trajectory control
- Now moving to **continuous manufacturing** for **personalised medicines**
 - PAT and digital models provide detailed understanding
 - Predictive models enable on-the-fly adjustment
 - True agility: assets tasked with **continuously changing recipes**



Lean Model Management

Development and Validation

Formulated Products

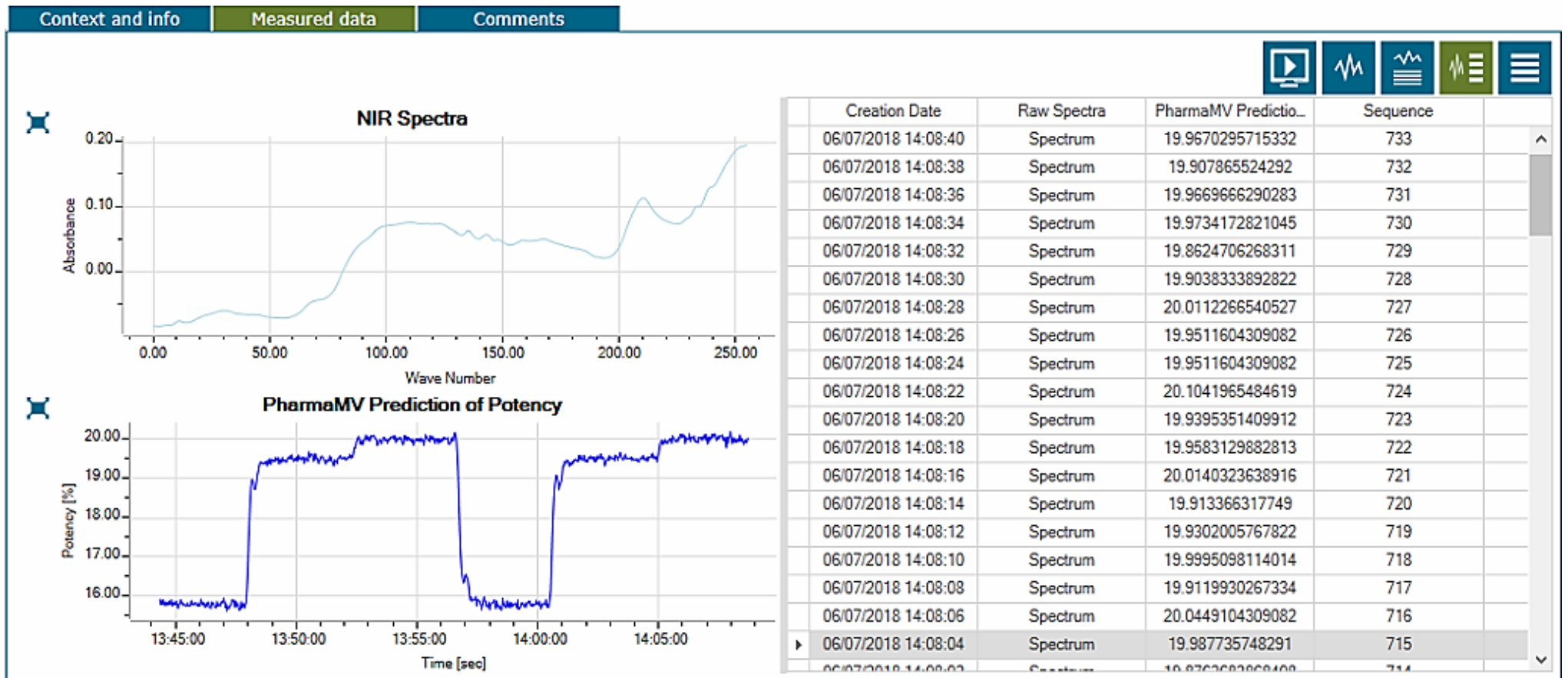
- Multiphase complex liquids
- CQA only available after ALL ingredients are added, mixed, blended
- CQA highly influenced by variations in
 - process design
 - operational parameters
 - raw material quality

Modelling

- First, model process responses
- Second, model impact of raw material variability on quality
- Third, ensure the models are robust enough for industrial application



Lean Model Management Development and Validation



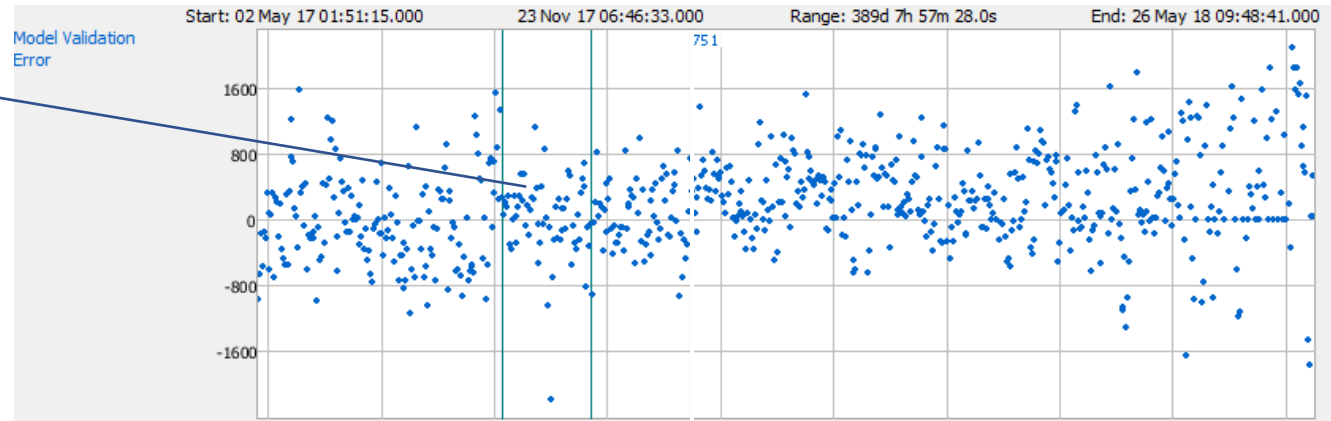
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Development and Validation

The most common mode of failure for an online model is prediction 'drift'

The easiest way to detect this is with a CUSUM chart

Rapidly identify point at which model needs to be re-tuned

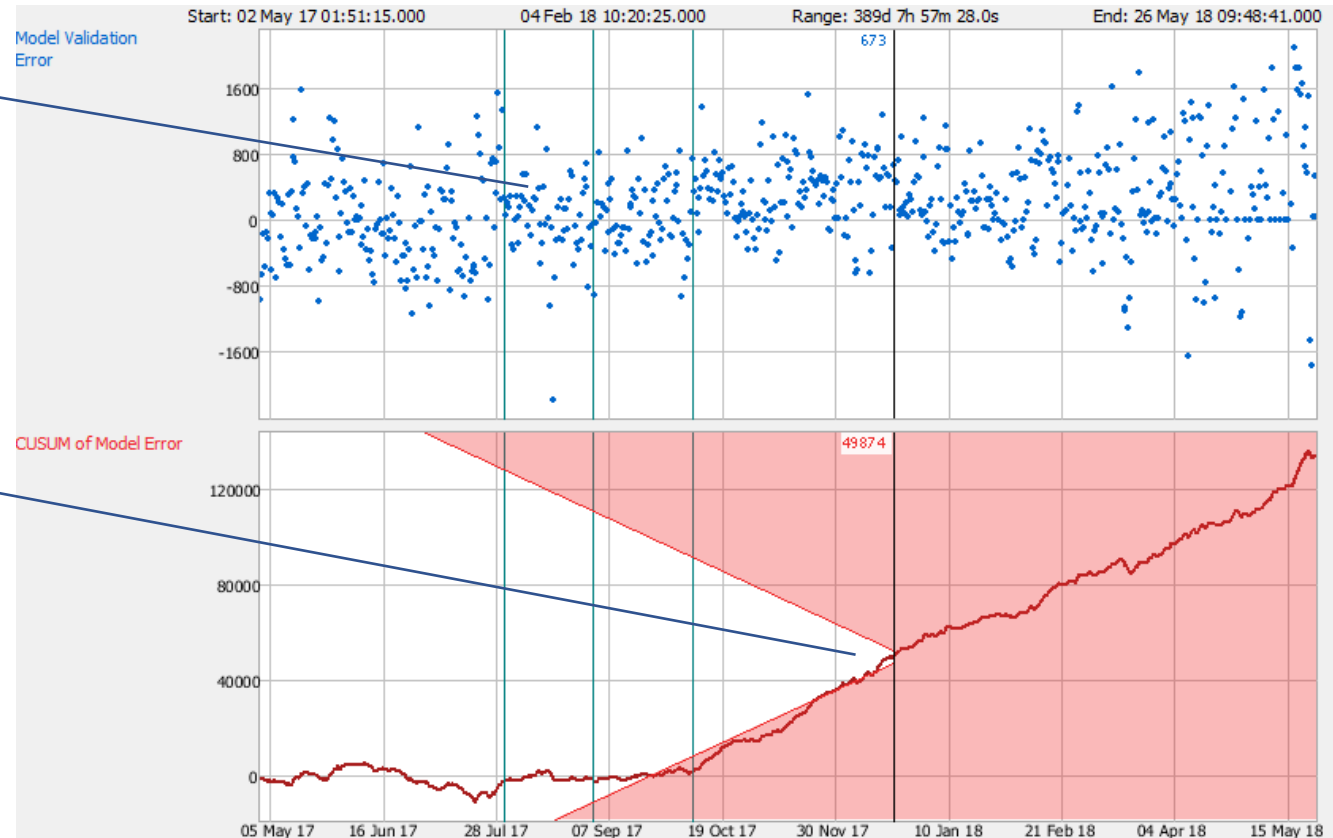


Lean Model Management

Development and Validation

If the CUSUM history fits within the 'jaws' of the VMask, then all is well

If CUSUM history is outside the VMask, model has drifted significantly – action is required



Lean Model Management Adaptation

Where do we Adapt?

- **New process** – no knowledge – needs human-input model development
- **Existing process** – scale-up, new product variant, process change – model may not fit

What do we Adapt?

- The control algorithms don't need to be changed, just how they are used
- The model needs to be changed, to provide better predictions to the controller

Why do we Adapt?

- No engineering resources to start from scratch
- No testing time available

Machine Learning

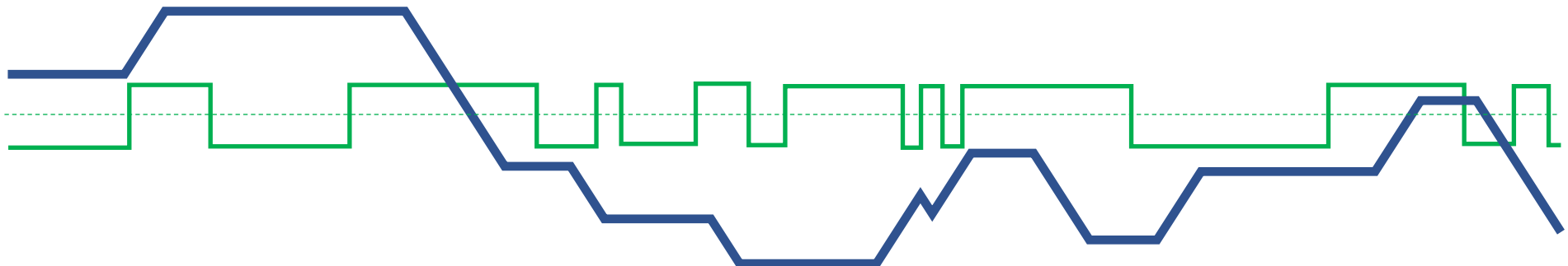
- Unsupervised model development



Lean Model Management Adaptation

Practical Application

- Control remains 'on' even though performance may not be optimal
- Small PRBS perturbation is added – smaller than existing control moves
- PRBS iteratively updates a second model in the background
- Adaptive algorithm 'knows' how the plant will behave with current model
- Mismatch between expected and actual behaviour generates adaptive model
- Only need to adapt those paths that need to be changed
- Process knowledge is key



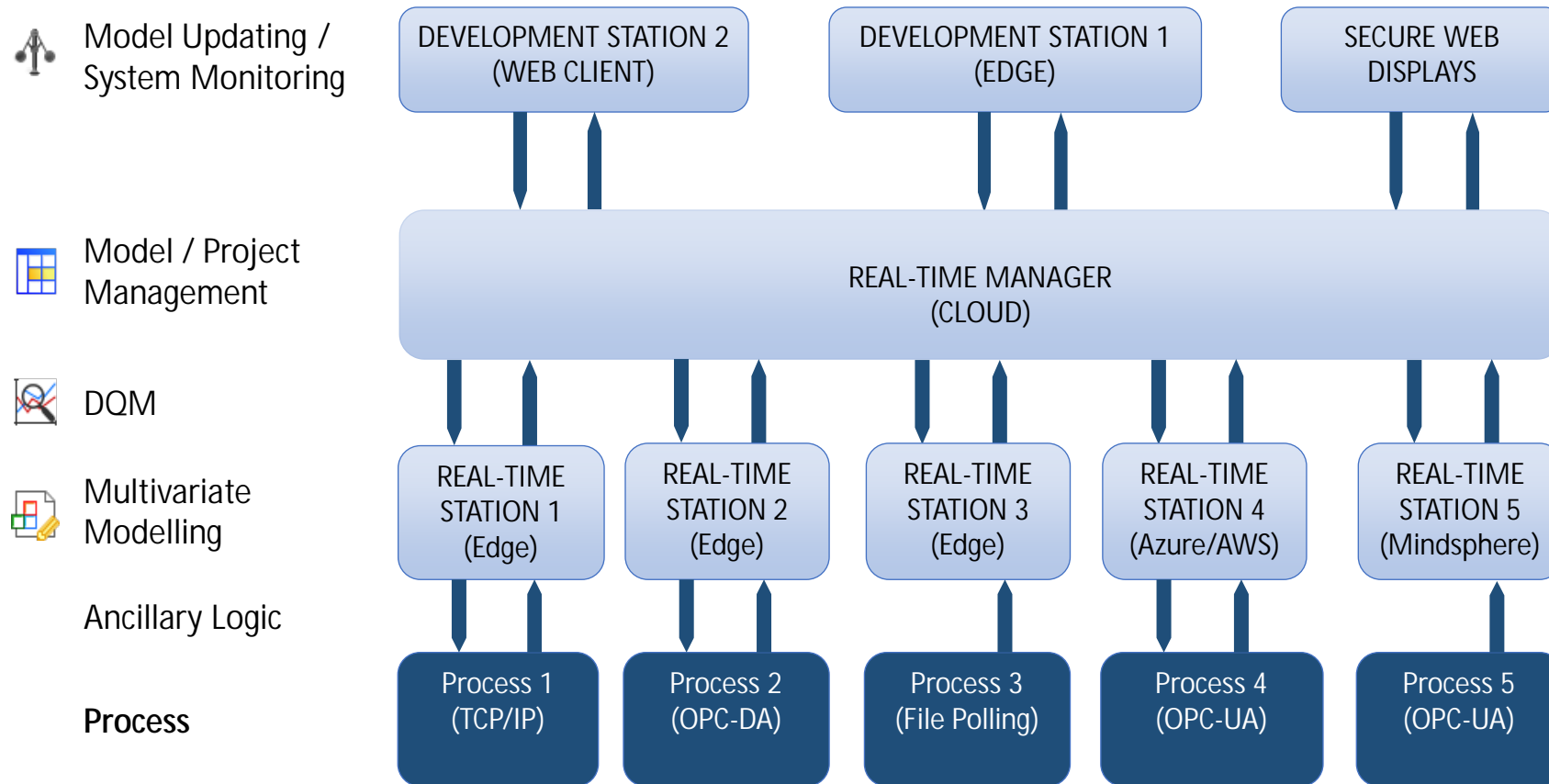
Cloud-Based Model Management Real Time Manager Architecture

Features

- A common platform for development and real time systems
- Encrypted, version-controlled project storage and deployment
- Mapped with recipe / product tables
- Data extraction and modelling using **PerceptiveAPC Development**
- Manage **PerceptiveAPC Real-Time** instances for:
 - Deploying Chemometrics
 - Continuous Process Verification (CPV)
 - Statistical Process Control (SPC)
 - Advanced Process Monitoring, Control, Optimisation
- OPC interface into process automation systems
- User-friendly customisable secure remote displays
 - can be embedded into production systems



Cloud-Based Model Management Real Time Manager Architecture



Lean Model Management

Dedicated Remote Interface for Each Station

Dissemination and Access

- Provide the **right** information
- To the **right** people
- **When** they need it
- Enabling full **interaction**

The image displays a software interface for an RT Station, divided into several sections:

- Navigation Bar (Top):** Three buttons labeled 'Offline', 'Online/Edit', and 'Online'. A red arrow points from this bar to a similar bar at the bottom.
- RT Station 1 (Top Panel):**
 - Status:** RT Station Status: No Method. Meas Enable: On. SCADA: Enable. Confirm. Alarm: OK. Watchdog: OK. Recipe/Method: -1, none. Lot Number: Lott_16072015. Product Description: APII. Product ID: X236_T53.
 - Quality Attributes:** Overall Product Status. ValQA1 (QA Variable 1): 0.0. ValQA2 (QA Variable 2): 0.0. ValQA3 (QA Variable 3): 0.0. ValQA4 (QA Variable 4): 0.0.
 - Other Attributes:** VarLatent1 (Latent Variable 1): 0.0. VarLatent2 (Latent Variable 2): 0.0. VarLatent3 (Latent Variable 3): 0.0. VarLatent4 (Latent Variable 4): 0.0. VarLatent5 (Latent Variable 5): 0.0.
- Instrument (Middle Panel):** A graph showing a spectral curve with a peak at 2100 nm and a value of 0.434. The x-axis ranges from 1100 nm to 2100 nm.
- RT Station 1 (Bottom Panel):**
 - Status:** RT Station Status: Measuring. Meas Enable: On. SCADA: Enable. Confirm. Alarm: OK. Watchdog: OK. Recipe/Method: 0, PAT_Template 2.2. Lot Number: Lott_16072015. Product Description: APII. Product ID: X236_T53.
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- Instrument (Bottom Panel):** A graph showing a spectral curve with a peak at 2100 nm and a value of 0.417. The x-axis ranges from 1100 nm to 2100 nm. A vertical line is drawn at 1668 nm with a value of 0.143.

Lean Model Management In Practice

Manufacture of Personal Care Products

- Ingredients added, blended
- Batch tested, adjusted, blended, re-tested repeat until passed

Real Time Release

- Predict end quality from process, quality & raw material data
- Validate prediction against lab & at-line QC results before first trial

Project Results

- Initial goal 40% RTR
- 25 mins saved per 2-hour batch
- Increase in saleable production capacity equates to seven-figure financial benefit p.a.



Lean Model Management In Practice

Current Status

- Some CQAs difficult to measure – low repeatability
- Model predictions are trusted more than tested results
- Any discrepancy – repeat tests and take average of 5 results

Current Status - Manufacturing

- Adjust recipes, change ingredients
- Broader number of products adjusted to 'fit' the models – virtuous circle
- Now running at 100% real time release

Future

- Multi-site roll-out
- Cloud-based data capture, analytics, model selection



Summary

Big Data

- No-one really wants big data
- Manufacturers want 'big knowledge' and, from that, 'big decisions'

With big data comes big responsibility

- Exponential increase in data
- Onus is on correct use of process models derived from that data
 - selection, validation, adaption and deployment
- Model management across distributed and disparate systems – what the cloud is for

Architecture

- AWS, Azure, MindSphere secure platforms for data collection and aggregation
- PerceptiveAPC – toolset for model development, validation, industrially-robust control
- Perceptive RT Manager – cloud-based management and model deployment





Thank you

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