



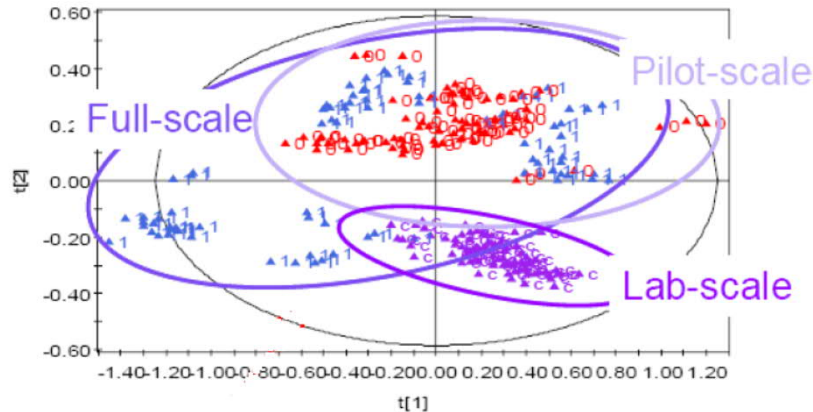
# **Integrated Control in Formulation Introduction to the Day**

**Julian Morris**

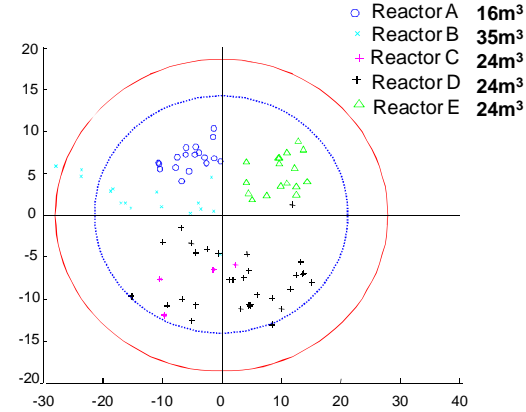
**Centre for Process Analytics & Control Technology  
Newcastle University & Strathclyde University, UK  
[www.cpact.com](http://www.cpact.com)**

**Towards Integrated Control in Formulations, CPT NetPark January 17<sup>th</sup> 2019**

# Coping with Process and Analytical Variability

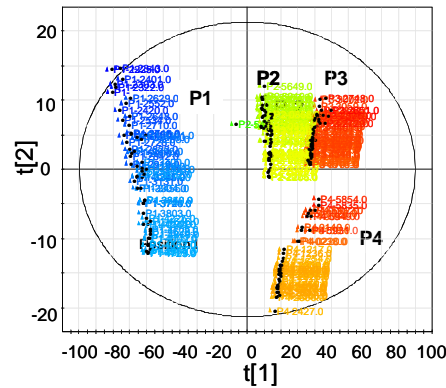
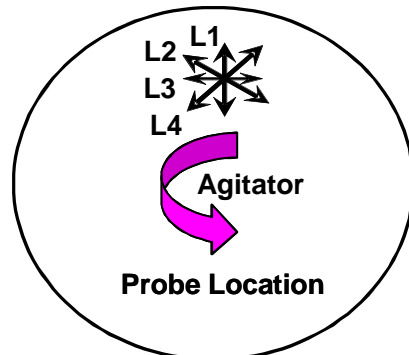


'Product Quality' across lab, pilot & production scales  
(Staffan Folestad AstraZeneca, AFACT09)

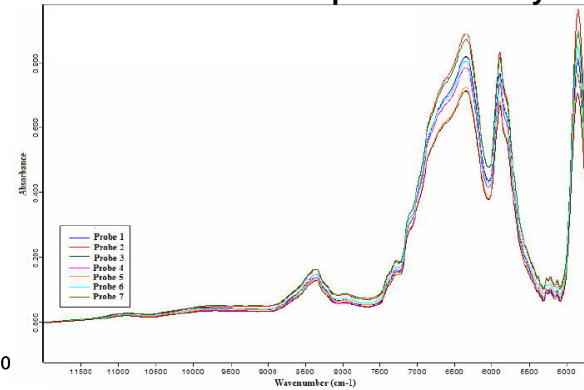


'Identical Reactors – Different heat-transfer characteristics ?'

Sensing space direction  
PCA of spectra collected for over 1 hr



Spectra from different probes show distinct Inter-probe variability



Courtesy R O'Kennedy et al (GSK & Univ)

## Challenges in Formulations Development and Production

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- Increasing new entity introductions & aggressive development cycles:
  - Wider range of product forms:
    - Reduced opportunity for generating data for analysis and modelling
- Demands a culture-change:
  - Products are **Complex** and **Multivariate**
  - Processes are **Dynamic** and **Time-varying**
  - Processes (e.g. reactions, ...) are **non-linear**
  - Products have '**Multivariate Distributions**'

## Collecting the Data Properly

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- W. Edwards Deming defined quality as: ***Good quality means a predictable degree of uniformity and dependability with a quality standard suited to the customer.***
  - ***Quality decisions must be based on quality data.***
- **‘Dirty Data’ Issues:**
  - Data compression
  - Outliers
  - Noise
  - Missing data
  - Distribution
  - Multivariable effects
  - Process Dynamics – auto-correlated measurements
  - Time Delays (eg off-line analysis)
  - Non-linearity
  - .....

## The Impact of Data Compression in Process Information Management Systems

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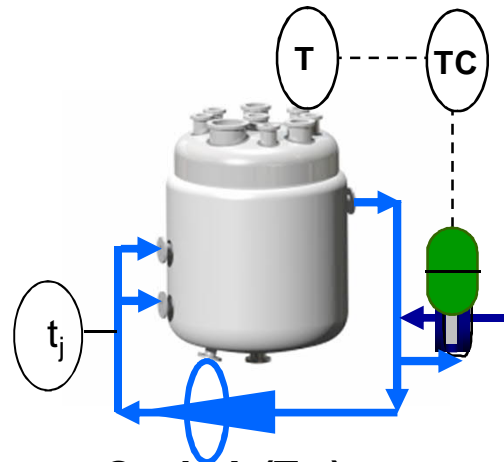
- ***Almost all commercial data historians compress the data before archiving.***
  - A question arises of how useful the compressed data are for the intended purposes – predictive modelling, calibration, process abnormality detection and diagnosis, data mining, .....?
  - It is (should be) widely known that data compression interferes with many types of data-driven analyses and the strong recommendation is of caution in the use of compressed process data archives and the need to ensure that any data compression limits are set to appropriate values to allow future assured analysis and use.

**A conservative data compression strategy is essential since missing data can never be reconstructed**

**The costs of data storage are also constantly decreasing**

# The Co-Flux Reactor: An Opportunity for Enhanced Formulations Development?

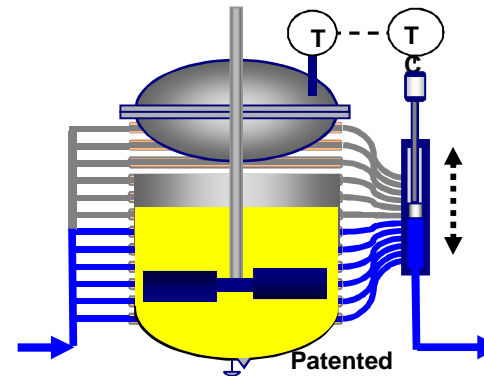
## Conventional control



$$Q = U.A.(T-t_j)$$

Jacket temperature controlled

## Coflux<sup>®</sup> control



$$Q = U.A.(T-t_j)$$

Jacket area controlled

Why use 'area' control?



1. Capable of very sensitive heat monitoring
2. Better temperature control
3. More energy efficient

As far as we know there are no current manufacturers of Co-flux reactors  
An opportunity for CPI Formulations to design and construct their own variant?