Dynamic Process Control: Implementation of Feedback/Feedforward Control for Continuous Systems

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Overview

• Introduction to Static & Dynamic System Analysis

• Continuous Processes – Examples of Process Dynamics

• Advanced Process Control in Continuous Pharmaceutical Processes

• Example Results from Continuous SOD processing

• New Platform Technology
Introduction & Terminology

Statics
- “Steady State” Conditions
- Initial vs Final States

Dynamics
- Transition Between States
- Change over Timer

System Behavior

Reality
- Superimposed dynamics & Statics
- Analysis must consider both
Static & Dynamic Response

The two systems identical in their Static response

But very different in terms of their Dynamic

Response to Setpoint Change
Dynamic Response

Process Gain = \frac{\Delta \text{output}}{\Delta \text{input}}

G(s) = \frac{Ke^{-t_ds}}{Ts + 1}

First Order System
Many continuous processes exhibit first order system dynamics.

First Order Systems Response to Input Change

Oscillatory response for under-damped systems

Over-damped Response
Typical Dynamic Responses of Continuous Solid Formulation Processes

Response Time: dependent on mixing/throughput parameters

Steady state fluctuations partially due to measurement errors caused by moving powder
APC in Continuous Processing

- Continuous processes are time dependent & may experience transient process upsets

- Fast PAT systems are essential to monitor real-time performance, and divert OOS material

A transient $\frac{1}{2}$ minute process upset, in a high throughput continuous Process can result in high volume of rejected OOS (eg. 5000 OOS units with throughput of 120 kg/hour)

(assumes 200mg dosage weight)
APC Architecture for Continuous Blending Applications

- **Throughput Setpoint**
- **Raw Materials Concentration Setpoints**
- **Initial Process Setpoints**

**Model Predictive APC**
- Feeders Ratios
- Impeller Speed
- Retention Mass

**Dynamic Setpoints**
- Blend Composition

**Multiple Feeders**
- Continuous Formulation System
- Load Cells Readings

**Feedforward Loops**
- Blend
- Retained Mass

**Feedback Loops**
- Load Cells

**Fast NIR System**
Feedback vs Feedforward

✓ Feedback Loops provide dynamic information on the process outputs error

✓ Feedback Loop Measurement Point (location) is critical for stability of control loops

✓ Large separation between measurement & Actuation points increases the response delay (dead-time)

✓ Feedforward loops are used to preemptively reduce the impact of dead-time and delay in system response to feeder excursions
Pfizer’s New Continuous SOD
Portable, Continuous, Miniature & Modular

Continuous Mixing
Direct Compression

Consigma™ -25
TSWG

Raw Material
Dispensing

Slide Courtesy: Dan Blackwood et al.
AIChE 2013
1. API Concentration is above target

2. Feeder performance adjusted to achieve target API Concentration

3. API Concentration by on-line NIR is centered at Target

Slide Curtesy: Dan Blackwood et al. AIChE 2013
1. API Potency is at target

2. Production has been increased from 3 to 3.5 kg/hr

3. Feeder Performance is adjusted

4. Hold Up Mass is held Constant

5. Potency setpoint change from 14 to 10%.

6. The APC implements the potency change while controlling production and hold-up mass to setpoint.

Slide Curtsey: Dan Blackwood et al. AIChE 2013
Real-time Material Characterization Platform
Capturing Process Signature
Real-time NIR Imaging System
Dynamic Process Signature

![Image of Real-time NIR Imaging System interface with graphs and images showing process data]
Hidden Process Fingerprint

Advanced Image Processing Algorithm for Visualization of Blend Lubrication, Micro Temp Variations & Environmental Impacts on Blend Performance

Visualization of MgSt dispersion and lubrication film in SOD Matrix
APC in Continuous Processing

- APC system can reduce the frequency and severity of transient excursions and associated cost impact

- In Pfizer, APC is rapidly gaining acceptance as a key enabling and transformational technology for both continuous and batch processes

- New platform technologies for real-time material characterization provide new capabilities for validation
Acknowledgement

- Pfizer PCMM Team
- Pfizer GTS Colleagues
- Pfizer AMT Colleagues