Population Balance Modelling of Twin Screw Wet Granulation in a Model Driven Design Framework

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Outline

• Background

• Generic Framework for Model Driven Design

• Twin Screw Granulation (TSG) of Consigma 1

• Twin Screw Granulation in gPROMS

• Population Balance Modelling of TSG

• Conclusions
Background

• Particulate process is ubiquitous in a wide spectrum of industries but poorly understood as compared to liquid and gas process.

• Particulate process modelling is increasingly used as a powerful means to accelerate the development of robust product.

• Too few particle based processing models are translated into industrial particulate processing due to the lack of process understanding.

• A project 'Models for Manufacturing of Particulate Products (MMPP)' was initiated by CPI taking twin screw granulation as exemplar for Model-Driven Design.
**Project Participant**

**Advanced Modelling Partners**
- PSE (Process System Enterprise)
- EDEM (DEM Solutions)

**Industry Partners**
- Pfizer
- AstraZeneca
- Johnson-Matthey
- Procter and Gamble

**Commercialising models - modelling platform/libraries – interfaces for model coupling**

**Knowledge Partners**
- Sheffield Univ.
- Edinburgh Univ.

**Project Management – Pathway to Exploitation**


**Know-how - provisional models – work-flow deve.- model validation – prototype model deve.**
Generic Framework for Model Driven Design

1. Identify Critical Quality Attributes (CQAs)
2. Model Conceptualisation
   - Proceed? NO
   - Model Verification
     - Verified? NO
3. System Characterisation
   - Multi-scale Modelling
     - Validated? NO
4. Multi-scale Model Results (e.g., GSD, RTD)
   - Calibrated Model Parameters
     - Established Uncertainty Simulation vs. Experiment
6. Defined Conceptual Model Development & Implementation
   - Resources & Feasible
     - Established Model Appropriateness
       - Verified? NO
7. Model Validation
   - Model Driven Design
     - Validated? YES

*Model Validation Cycle* for New Processes: YES
- Update during lifecycle as components change
- NO

*Model Validation Cycle* for Modified Processes: NO
- Proceed? YES

*Critical Quality Attributes*:
- Defined Conceptual Model
- Model Appropriateness
- Calibrated Model Parameters
- Multi-scale Model Results (e.g., GSD, RTD)
- Simulation vs. Experiment

*Outcomes*:
- Model Driven Design (YES)
- Multi-scale Modelling (NO)
- Model Validation (NO
- System Characterisation (NO)
Generic Framework for DEM-PBM coupling

- Generic Framework that can be applied to many different industrial systems.
GEA ConsiGma 1 Twin Screw Granulator (TSG)
Module of Twin Screw Granulation in gPROMS

- Customize modelling kernels for TSG
- Sensitivity analysis of defined PBM model
- Function to validate the PBM results against TSG data
- Master of coupling framework between DEM and PBM
Population Balance Model

A 3-D dimensional population balance model to simulate the evolution of granule attributes over time is given:

\[
\frac{\partial}{\partial t} n(s,l,g,t) + \frac{\partial}{\partial s} \left[ n(s,l,g,t) \frac{ds}{dt} \right] + \frac{\partial}{\partial l} \left[ n(s,l,g,t) \frac{dl}{dt} \right] + \frac{\partial}{\partial g} \left[ n(s,l,g,t) \frac{dg}{dt} \right] = B_{\text{nuc}}(s,l,g,t) + B_{\text{break}}(s,l,g,t) - D_{\text{break}}(s,l,g,t) + F_{\text{in}} - F_{\text{out}}
\]

- \( n(s,l,g,t) \): population density (a function of particle volume)
- \( \frac{\partial}{\partial s}, \frac{\partial}{\partial l}, \frac{\partial}{\partial g} \): state change due to layering, liquid addition and consolidation
- \( B_{\text{nuc}}(s,l,g,t) \): birth rate due to drop nucleation
- \( B_{\text{break}}(s,l,g,t) \) and \( D_{\text{break}}(s,l,g,t) \): birth and death due to breakage
- \( F_{\text{in}} \) and \( F_{\text{out}} \): Inlet and outlet flow rates in the unit
A compartmental approach used to evaluate material transport along the granulator and the outlet flow rate is given by:

\[ F'_{\text{out}} = \frac{F}{\tau} \]

where \( F'_{\text{out}} \) is the outlet flow rate of the unit; \( F \) is mass in the unit; \( \tau \) is residence time in the unit.

It is assumed that material only flows in one direction and the inlet flow rates are equal to the outlet flow rates of the previous compartments.

- The residence time \( \tau \) would be estimated from DEM (Barrasso and Ramachandran, 2016)
- Appropriate kernels are chosen for each compartment based on assumed phenomena in each compartment.
Residence Time Estimation from EDEM

- Particle generation by dynamic factory
  - Particles travel full length of screw
  - Computationally expensive
  - Shortened version tested where factory is moved closer to liquid addition point

Material flow

Credit: Courtesy by Dr. JP Morrissey from University of Edinburgh
Breakage in PBM

The breakage equation in PBM is given:

\[
\frac{dM(i, t)}{dt} = \int_{i}^{\infty} S_M(j)b_M(i, j) dj - S_M(i)M(i, t)
\]

- The selection function $S_M$ and the breakage function $b_M(i, j)$ are the two important functions
- $M(i, t)$: mass of particles with volume $i$ at the time $t$
- $S_M(i)$ and $S_M(j)$: specific breakage rates of mass fraction of particles of volume $i$ and $j$
- $b_M(i, j)$: fragment size distribution probability between the volume range $i$ and $j$
- $b_M(i, j) = B_{i-1,j} - B_{i-1,i}$
PBM Kernels for TSG

- Model assumption in gPROMS TSG library is improved by implementing custom kernels that are TSG specific and distinguish the chipping and fragmentation in conveying and kneading elements respectively. The advantage of the developed breakage model accounts for the key parameters:
  - powder feed number
  - dynamics strength
  - maximum breakage size

- Coupled with DEM simulations to provide RTD, rather than experimental mean

- Key parameters are identified through the use of GSA (Global system analysis), which significantly reduces the amount of parameters for validation
Breakage rate process isolating experiments

9 different model material systems with two orders of magnitude variation in dynamic yield strength

- Breakage characterisation in CE and DMX
- Critical breakage size determined from the geometry gap
Breakage Test in Screw Elements

- Breakage pattern is dramatic in conveying and mixing elements
- Granules start breakage earlier in the distributive mixing elements
- The critical lower breakage size in conveying element is bigger than that in mixing elements
- New model is required to interpret such behaviour

After Pradhan et al. 2017
Breakage Pattern in TSG

- Chipping is subsurface material removal due to local damage and approximately follows the power law as a function of particle size in conveying element.

- Fragmentation (crushing) is splitting of the original particle into many pieces and approximately follows the Weibull law in kneading/distributive mixing element.
Selection Function Development in CE and DME

\[
\frac{dM(v,t)}{dt} = \int_v^\infty S_M(w)b_M(v,w)dw - S_M(v)M(v,t)
\]

- **Chipping**
  \[S_M = a \times \exp[b \times PFN \times DYS]\]

- **Fragmentation**
  \[S_M = a \times (\exp[-b \times PFN \times DYS]) + (1 - a)\]

*Powder Feed Number (PFN) = \(\frac{m_{\text{powder}}}{\rho_{\text{bulk}} \cdot D^4}\)*
Breakage Function Development in CE and DME

- Previous breakage function: two halved particles
- Weibull size distribution fits well for both chipping and fragmentation in CE and DME

\[ B_M = \begin{cases} 
1 & x > x_{uc} \\
1 - \exp\left(-m \cdot \left(\frac{x}{x_{uc}}\right)^n\right) & x_{lc} < x < x_{uc} \\
0 & x < x_{lc} 
\end{cases} \]
Breakage Kernel

**Selection function**

\[
S_M = S_{cM} \begin{cases} 
1 & x > x_{uc} \\
0 & x < x_{lc} 
\end{cases}
\]

**Kneading element**

\[
B_M = \begin{cases} 
1 & x > x_{uc} \\
1 - \exp\left(-m \left(\frac{x}{x_{uc}}\right)^n\right) & x_{lc} < x < x_{uc} \\
0 & x < x_{lc} 
\end{cases}
\]

**Conveying element**

\[
S_M = S_{cM} \begin{cases} 
1 & x > x_{uc} \\
0 & x < x_{lc} 
\end{cases}
\]

Modified Weibull distribution

*Pradhan et al. 2017, Granule breakage in twin screw granulation: Effect of material properties and screw element geometry*
Modelling Kernel Formation

**Nucleation**

\[ D_{mp, nuc} = \frac{L_{in, powder}(x, t)}{V_{droplet}}(1 - \varepsilon_{bed})V_{nuc} \]

Barrasso and Ramachandran, 2015

**Layering**

\[ G = G_m \frac{M_{powder}}{k M_{granule} + M_{powder}} \exp \left[ - a(x_w - x_{wc})^2 \right] \]

Cameron et al., 2005

**Breakage**

\[ S_M = \begin{cases} 
1 & x > x_{uc} \\
\frac{f_n(DYS, PFN, \text{etc.})}{x_{crit}} & x_{tc} < x < x_{uc} \\
0 & x < x_{tc}
\end{cases} \]

\[ B_M = \begin{cases} 
1 & x > x_{uc} \\
1 - \exp(-a \cdot \frac{x}{x_{crit}}) & x_{tc} < x < x_{uc} \\
0 & x < x_{tc}
\end{cases} \]

**Consolidation**

\[ \frac{d\varepsilon}{dt} = -k(\varepsilon - \varepsilon_{min}) \]

Iveson et al., 1996

Rate Processing Kernels

Conveying: addition port

Conveying/Kneading

Kneading
PBM Parameters Category

Input PBM Model Parameters

- Material properties
  - PSD
  - Bulk density
  - Shape factor
  - Intra-particle void etc.

- TSG geometry
  - Screw dimension
  - No. of conveying & kneading elements

- Process parameters
  - L/S ratio
  - Material feed rate
  - Mean residence time

- Rate constants
  - Nucleation
  - Layering
  - Breakage
  - Consolidation
## PBM Input Parameters

<table>
<thead>
<tr>
<th>Material parameters</th>
<th>Process parameters</th>
<th>Selection function parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSD: 40-180 µm</td>
<td>Powder feed rate: 14.4 kg/h</td>
<td>Breakage rate constant: 1.3 (2 in KE)</td>
</tr>
<tr>
<td>Shape factor Volumetric = 0.524</td>
<td>L/S ratio: 0.1-0.3</td>
<td>Minimum critical particle size:</td>
</tr>
<tr>
<td>Shape factor Surface = 3.141</td>
<td>Mean residence time (CE) = 0.051 s/cm</td>
<td>1600 µm for conveying</td>
</tr>
<tr>
<td>Etc.</td>
<td>Mean residence time (KE) = 0.089 s/cm</td>
<td>1200 µm for kneading</td>
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<tr>
<td></td>
<td></td>
<td>Maximum critical particle size:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3500 µm for conveying</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3200 µm for kneading</td>
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<tr>
<td></td>
<td></td>
<td>Size exponent: 1.2</td>
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<tr>
<td></td>
<td></td>
<td>PFN: 0.011</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DYS: 10 kPa</td>
</tr>
</tbody>
</table>

### TSG parameters
- Conveying 1.0 = 25.4 mm
- Conveying 1.5 = 38.1 mm
- Conveying 2.0 = 50.8 mm
- Kneading 1/4 and 1/6 inch

### Breakage function parameters
- Weibull distribution
- Scale exponent: 2 (6 in CE)
- Shape exponent: 2 (6 in CE)
Global System Analysis (GSA)

From point calculation to global system analysis (After Costas Pantelides, 2016)
Global System Analysis (GSA)

Discrete point calculation  ➔  Global system analysis
Global System Analysis (GSA)

Global system analysis of droplet size

Global system analysis of growth rate
## Leverage of PBM Input Parameters using GSA

<table>
<thead>
<tr>
<th>Rate Parameters</th>
<th>Kernel</th>
<th>Influence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean droplet size</td>
<td>Nuc.</td>
<td>Large</td>
</tr>
<tr>
<td>Nucleus pore saturation</td>
<td>Nuc.</td>
<td>Large</td>
</tr>
<tr>
<td>Std of droplet size</td>
<td>Nuc.</td>
<td>Medium</td>
</tr>
<tr>
<td>Max growth rate</td>
<td>Layering</td>
<td>Medium</td>
</tr>
<tr>
<td>Min moisture content</td>
<td>Layering</td>
<td>Small</td>
</tr>
<tr>
<td>Kinetic a</td>
<td>Layering</td>
<td>Small</td>
</tr>
<tr>
<td>Kinetic k</td>
<td>Layering</td>
<td>Small</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rate Parameters</th>
<th>Kernel</th>
<th>Influence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakage rate</td>
<td>Breakage</td>
<td>Large</td>
</tr>
<tr>
<td>Size exponent</td>
<td>Breakage</td>
<td>Large</td>
</tr>
<tr>
<td>Min critical size</td>
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<td>Medium</td>
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<tr>
<td>Max critical size</td>
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</tr>
<tr>
<td>DYS</td>
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<td>Medium</td>
</tr>
<tr>
<td>PFN</td>
<td>Breakage</td>
<td>Medium</td>
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<tr>
<td>Parameter a</td>
<td>Breakage</td>
<td>Medium</td>
</tr>
<tr>
<td>Parameter b</td>
<td>Breakage</td>
<td>Medium</td>
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</table>

<table>
<thead>
<tr>
<th>Rate Parameters</th>
<th>Kernel</th>
<th>Influence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scale m</td>
<td>Breakage</td>
<td>Large</td>
</tr>
<tr>
<td>Scale n</td>
<td>Breakage</td>
<td>Large</td>
</tr>
<tr>
<td>Cons. rate</td>
<td>Cons.</td>
<td>Small</td>
</tr>
<tr>
<td>Minimum porosity</td>
<td>Cons.</td>
<td>Small</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Process parameters</th>
<th>Kernel</th>
<th>Influence</th>
</tr>
</thead>
<tbody>
<tr>
<td>L/S ratio</td>
<td>NA</td>
<td>Large</td>
</tr>
<tr>
<td>Average RTD</td>
<td>NA</td>
<td>Large</td>
</tr>
</tbody>
</table>
TSG Setup

Consigma 25

Granule outlet

Liquid inlet

Powder inlet

Screw configuration

Configuration 1

Kneading element

Configuration 2

Kneading element

Configuration 3
Granulation Test Conducted in AZ

<table>
<thead>
<tr>
<th>Run</th>
<th>Feed Rate (kg/hr)</th>
<th>Screw Speed (RPM)</th>
<th>Screw Configuration</th>
<th>L/S Ratio</th>
<th>Attribute to measure</th>
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</thead>
<tbody>
<tr>
<td>Group 1 (Calibration)</td>
<td>14</td>
<td>600</td>
<td>C1:CE</td>
<td>0.15</td>
<td>GSD Porosity</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>0.25</td>
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<td></td>
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<td></td>
<td></td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>Group 2 (Calibration)</td>
<td>14</td>
<td>600</td>
<td>C1+KE: 6x60F</td>
<td>0.15</td>
<td>GSD Porosity</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>0.25</td>
<td></td>
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<td></td>
<td>0.35</td>
<td></td>
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<tr>
<td>Group 3 (Validation)</td>
<td>14</td>
<td>600</td>
<td>C1+2KE: 6x60F</td>
<td>0.15</td>
<td>GSD Porosity</td>
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<tr>
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<td></td>
<td>0.25</td>
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<td></td>
<td></td>
<td>0.35</td>
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</tr>
</tbody>
</table>
Observations from DEMC LSR 0.35

Granule collection pan
(DEMC LSR 0.35)

Powder/Paste distribution along the granulator

Kneading element
Conveying element
Flowchart for PBM Model Validation

In CE Configuration
Define the influential $D_{mic}$, $\epsilon_{bed}$, $S_{CM}$, $x_{ci}$, $G_m$

In CE Configuration
Model validation for LSRs 0.15 0.25 0.35

For Screw Configurations by DoE
Adjust the most influential parameters

Modelling & Validation Cycle
Per material / formulation

In C1+KE
adjust $S_{cm}$, $x_{ci}$ in KE
ALL OTHER CONSTANT

In C1+KE
Model Validation
LSRs 0.15, 0.25, 0.35

Test DEMC
LSRs 0.15 0.25 0.35
NO ADJUSTABLE Parameters

Calibrated?

YES

NO

Validated?

YES

NO

Predict New Configuration beyond Experimental Space
1st Calibration Stage (Conveying Only)

Experimental Result

DEM+PBM Calibration Result
2nd Calibration Stage (Conveying & 1 Kneading Block)

Experimental Result

DEM+PBM Calibration Result
Group 3 - Full Configuration Validation results

Experimental Result

DEM+PBM Validation Result
Conclusions

- PBM model could be simplified by identifying the influential parameters through global system analysis
- Nucleation and breakage are the two dominant mechanisms for granule production whilst layering and consolidation are inconspicuous
- Particle scale DEM is useful to provide the RT with further efforts for alternative numerical-based kernel based on particle dynamics
- Model parameters should be categorized and carefully chosen to minimise the amount of fitting parameters for model validation
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Thanks for your attention!