Population Balance Models for Granulation Process Design

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Acknowledgments

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Outline

• Introduction to granulation processes
• Modelling coalescence
  – A little bit of history
  – Multidimensional PBM
• Modelling nucleation and layering
Size enlargement by granulation

- Liquid binder used to form interparticle bonds
- Agitation of “wet mass” to promote liquid binder dispersion and granule growth
- Fluid beds, tumbling drums, mixers
Granulation equipment

- Mixer
- Spray Nozzle
- Chopper
- Impeller
- Fluid Bed
- Fluidising air
- Tumbling drum
Powder flow in a mixer granulator
Particle Design Principles

Product Engineering
- Developing the formulation

Process Engineering
- Process choice, design & scale up

Designer particle with controlled properties
(size, porosity, ....)
Granulation Rate Processes

1) wetting, nucleation and binder distribution

2) consolidation and growth

3) attrition and breakage

(Ennis & Litster, 1997)
Granulation rate processes

Controlling groups are known for nucleation and growth. Regime maps are available.
Current status for design

Measure Formulation Properties:

\[ d_p, \gamma \cos \theta, \mu, Y, \ldots \ldots \]

Estimate Process parameters:

\[ U_c, R\omega, \ldots \ldots \]

Calculate important dimensionless groups:

\[ \psi_a, t_p, St_{def}, S, \ldots \ldots \]

- Formulation design
- Process choice
- Rational scale up
- Trouble shooting
An Engineering Design Approach

Measure Formulation Properties: 
\(d_p, \gamma \cos \theta, \mu, Y, \ldots\)

Rate expressions

Population balance model

Granule properties
- Size distribution
- Density
- Strength
- Dissolution
- \ldots

Estimate Process parameters: 
\(U_c, R \omega, \ldots\)
Meso scale modelling of granulation processes

- Population balance models can track product attributes:

\[
\frac{\partial V_n(x,t)}{\partial t} = \dot{Q}_{in} n_{in}(x) - \dot{Q}_{ex} n_{ex}(x) - V \frac{\partial G_n(x,t)}{\partial x} + V b(x) - V d(x)
\]

\[
\frac{\partial V_n(v,t)}{\partial t} = \dot{Q}_{in} n_{in}(v) - \dot{Q}_{ex} n_{ex}(v) - V \frac{\partial (G^* - A^*)n(v,t)}{\partial v} + V (\dot{b}(v)_{nuc} + \dot{b}(v)_{coal} + \dot{b}(v)_{br} - \dot{d}(v)_{coal} - \dot{d}(v)_{br})
\]
A little bit of history

Ennis et al. (1991) first to focus on effect of granule properties

Early work by Kapur, Sastry and Fuerstenau focused on coalescence

\[ St_v < St^* \Rightarrow \text{granules will coalesce} \]

\[ St_v = \frac{4 \rho_g U_c d_g}{9 \mu} \]

\[ St^* = \left(1 + \frac{1}{e_r}\right) \ln\left(\frac{h_b}{h_a}\right) \]
A little bit of history


\[
kt_{\text{max}} = 6 \ln \left( \frac{St \times 9 \mu}{8 \rho_g \mu c d_0} \right) \propto \ln \left( \frac{\mu}{\rho_g \mu c d_0} \right)
\]

Adetayo and Ennis, 1998

\[
\beta(u,v) = \begin{cases} 
    k_o, & w < w^* \\
    0, & w > w^*
\end{cases} \text{ where } w = \left( \frac{uv}{u+v} \right)^b
\]
Modelling Coalescence

Type I: \[ St_V < \ln\left(\frac{h_0}{h_a}\right) \]

Type II: \[
\left(\frac{Y_d}{E^*}\right)^{1/2} \left(St_{def}\right)^{-9/8} < \frac{0.172}{St_{vis}} \left(\frac{\bar{D}}{h_0}\right)^2 \left[1 - St_{vis} \ln\left(\frac{h_0}{h_a}\right)\right]^{5/4} \left(\frac{h_0^2}{h_a^2} - 1\right)\]

The diagram illustrates the relationship between the dimensionless parameters and granule size distribution. The parameters are:

- $St_v = \frac{8mU_0}{(3\pi\mu D^2)}$
- $St_{def} = \frac{0.5mU_0^2}{(D^3\gamma_d)}$

The critical conditions for Type I and Type II coalescence are indicated by the curves $\beta = \beta_1$ and $\beta = \beta_2$, with $\beta = 0$ representing the rebound condition.

The graph compares the experimental data (exp.) and model predictions for different revolution counts (100, 300, 400, 500 rev.) with the initial size distribution (dotted line).

Liu & Litster, 2002
Multidimensional PB models

- Tracks the distribution $n(s,l,g)$

$$\frac{\partial Vn(s,l,g,t)}{\partial t} + \frac{\partial VG_s n(s,l,g,t)}{\partial s} + \frac{\partial VG_l n(s,l,g,t)}{\partial l} + \frac{\partial VG_g n(s,l,g,t)}{\partial g}$$

$$= \dot{Q}_{in} n_{in}(s,l,g,t) - \dot{Q}_{ex} n_{ex}(s,l,g,t) + V(\dot{b}(s,l,g,t)_{nuc} + \dot{b}(s,l,g,t)_{coal}$$

$$+ \dot{b}(s,l,g,t)_{br} - \dot{d}(s,l,g,t)_{coal} - \dot{d}(s,l,g,t)_{br})$$

- Challenge for efficient numerical solution
- Challenge for experimental validation
Evolution of Two-Dimensional Distribution

- Simulation result
  - binder-to-solids ratio of 0.11

\[ t = 0 \text{ s} \]

\[ t = 900 \text{ s} \]

\[ t = 300 \text{ s} \]

Ramchandran et al., (2008) - clear evidence of multi-dimensional heterogeneity

**Batch Granulation Results**

Granule size distribution

- binder-to-solid ratio = 0.125
- drum load = 1.75 kg

Binder content distribution

Porosity distribution
• Multidimensional PB approaches:
  – allow incorporation of more physics in the rate expressions
  – Track property distributions of interest to us
• But powder flow and particle interactions still represented in a crude, lumped parameter format
The impact of mixing and powder flow
PEPT results (600 rpm)

Impeller speed = 6.6 ms\(^{-1}\)
Average speed = 0.84 ms\(^{-1}\)
Maximum speed = 2.95 ms\(^{-1}\)
Regions for granulation rate processes
PEPT derived powder flow data

• Data required for models
  – Occupancy ✓
  – Velocity field ✓
  – Fluxes ✓
  – Stresses ✗
  – Collision frequencies ✗
  – Predictive ✗
Multiscale modelling
Parameter sensitivity

Dimensionless Contact Stiffness, $k^* = k/(\rho d^3 \gamma)$

Normal Collision Velocity (m/s)

Probability Density (m/s)$^1$

Ben Freireich (2008)
Shear Rate, & Solid Fraction

Collision Velocity Distribution
Drum Simulation
Baseline Conditions

Collision Velocity Density
Shear Simulation
$\nu = 0.55 \gamma = 15.0$

Dimensionless Normal Impact Velocity = $v_n/(\omega R)$

Dimensionless Tangential Impact Velocity = $v_s/(\omega R)$
• Area of drops compared to area sprayed, at a flowrate $V$ and a powder flux $A$ and drop size $d_d$

$$
\Psi_a = \frac{3V}{2 A d_d}
$$

• Low spray flux means a narrow nuclei distribution as most drops are well separated.

• Fraction of nuclei formed by 2 or more drops

$$
f_{multi} = 1 - \exp(-4\psi_a)
$$
Modelling Nucleation

• Purely drop controlled:
  \[ \dot{b}(v)_{\text{nuc}} = S n_s (s \varepsilon v) \]

• Extension to allow for non-uniform (real) sprays and some drop overlap using Monte Carlo simulation

Wildeboer, 2002
Modelling consolidation and layering

- Consolidating granules pick up fines (layering) as liquid is squeezed to the surface.
- When fines are used up, coalescence may start.

\[
G(v) = -k_{con} v \frac{\varepsilon - \varepsilon_{min}}{\varepsilon}
\]

\[
k_{con} = f(St_{def})
\]

- Predict induction time in batch systems.

Wildeboer, 2002
2-D distribution for layering

Mort et al., 2008
And now for something completely different: From this......
Design and control of physically regime separated continuous granulators

Stage 1: Wetting and Nucleation

Drop controlled Nucleation

Shear controlled Nucleation

Control parameters

Control parameters

Control parameters

Stage 2: Densification and growth

Densification and Layering

Densification and Coalescence

Regime separated granulators – Hans Wildeboer

- New nucleation device to give nearly monosized nuclei granules
  - Acoustic controlled showerhead over a thin bed of powder on a conveyor belt
  - Effectiveness depends on drop-drop and drop powder interactions at the powder surface
  - Extremely narrow size distributions possible
Summary