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 '**M**odels for **M**anufacturing of **P**articulate **P**roducts (**MMPP**)' was initiated by CPI taking twin screw granulation as exemplar for Model-Driven Design

Project Participant

Know-how – Data – Materials Characterisation - Materials – Work Flows

Industry Partners

- Pfizer
- AstraZeneca
- Johnson-Matthey
- Procter and Gamble

Advanced Modelling Partners

- PSE (Process System Enterprise)
- EDEM (DEM Solutions)

Project Management – Pathway to Exploitation

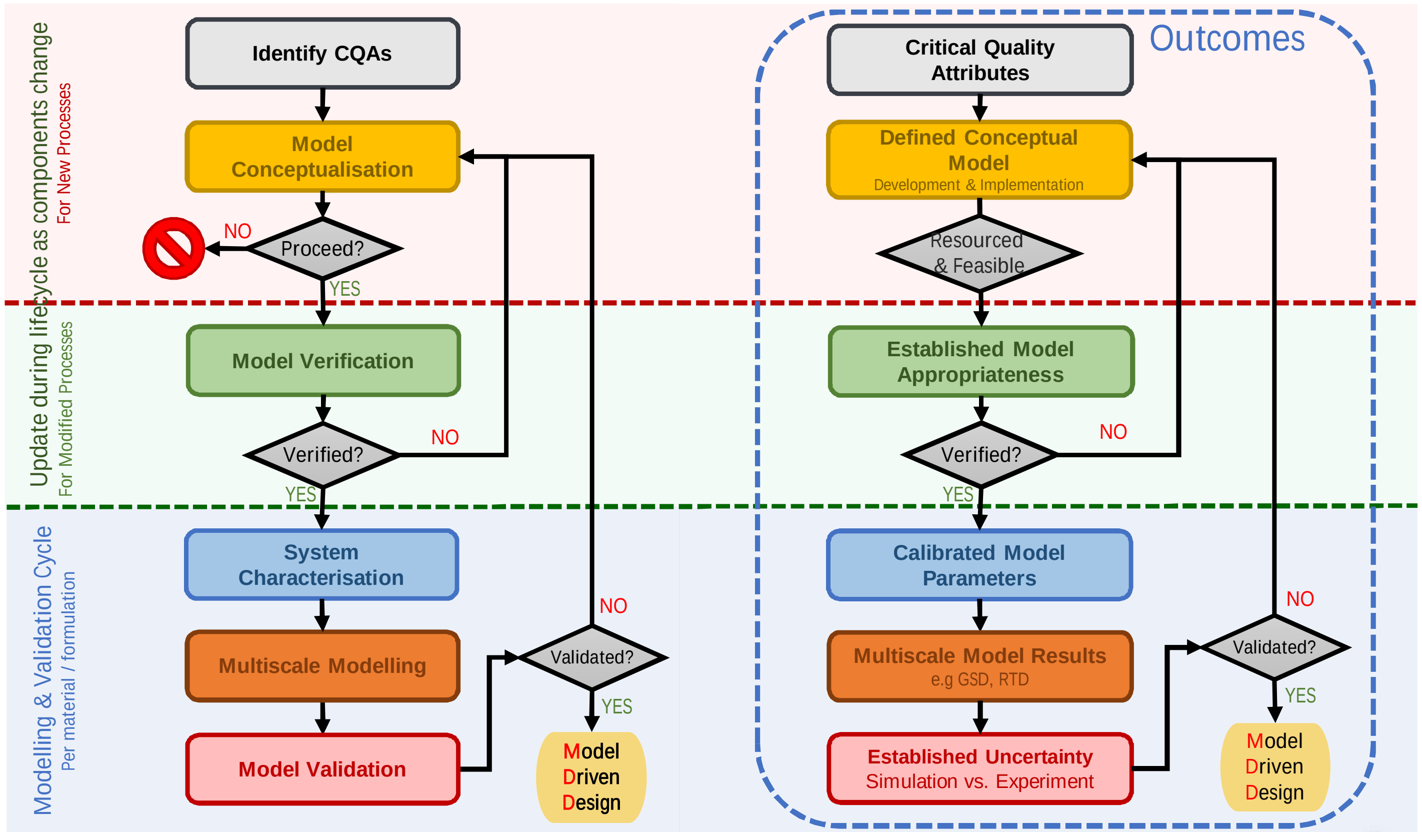
Commercialising models - modelling platform/libraries – interfaces for model coupling

Know-how - provisional models – work-flow deve.- model validation – prototype model deve.

Knowledge Partners

- Sheffield Univ.
- Edinburgh Univ.

Generic Framework for Model Driven Design



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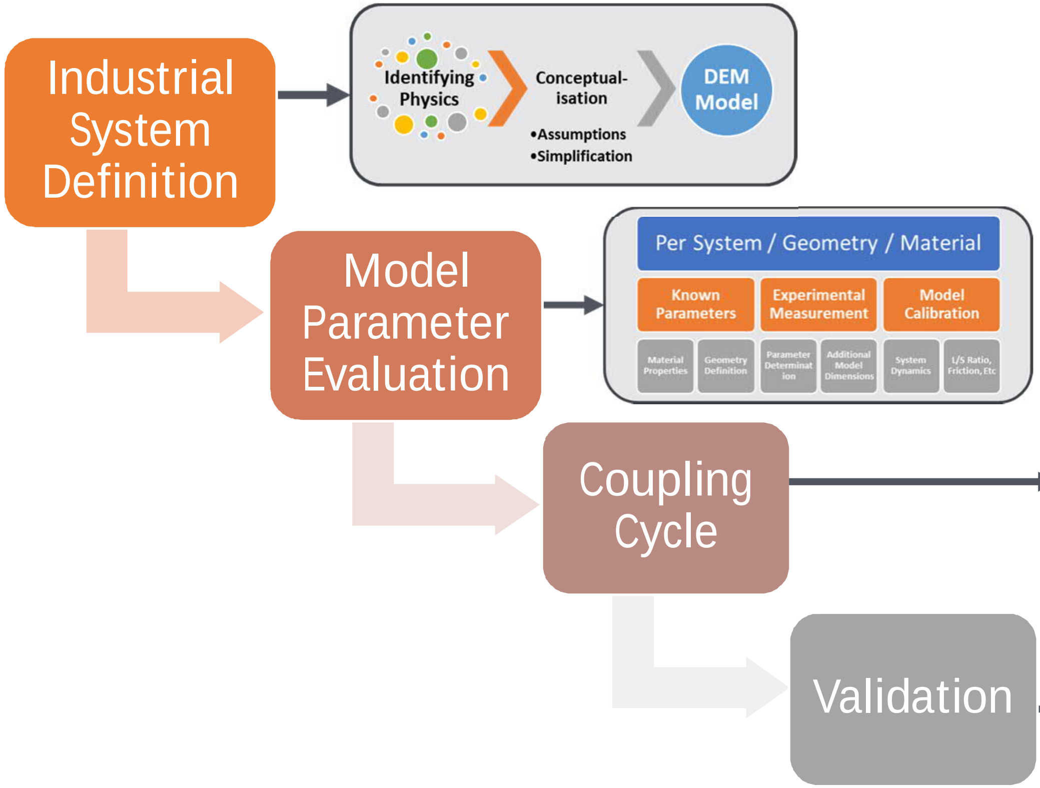
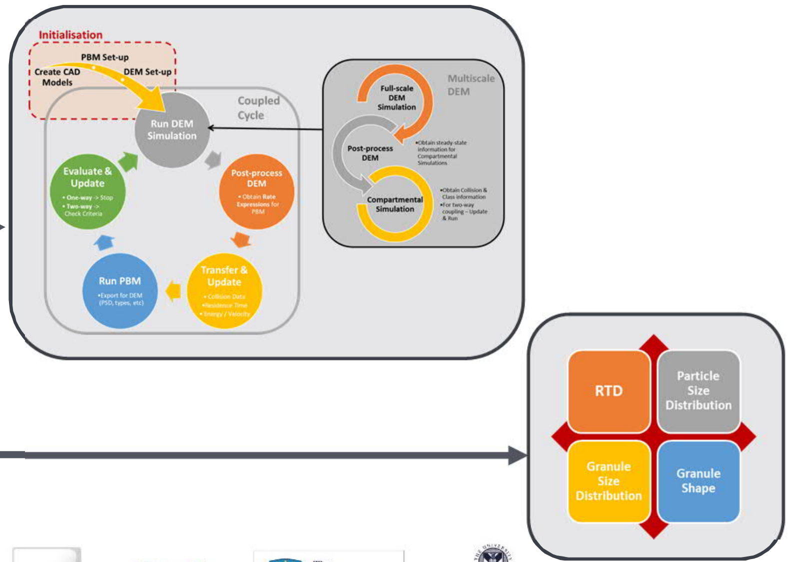
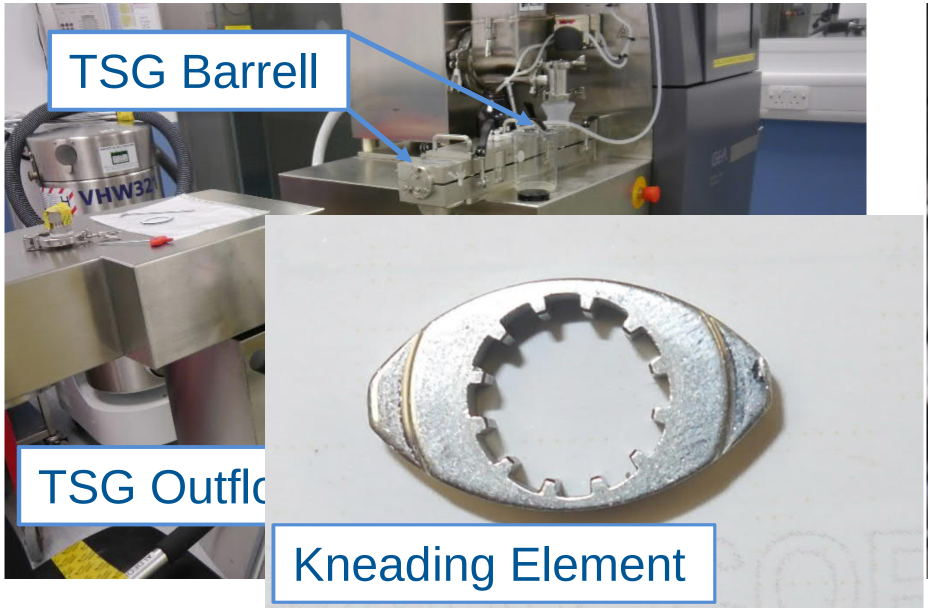
Generic Framework for DEM-PBM coupling

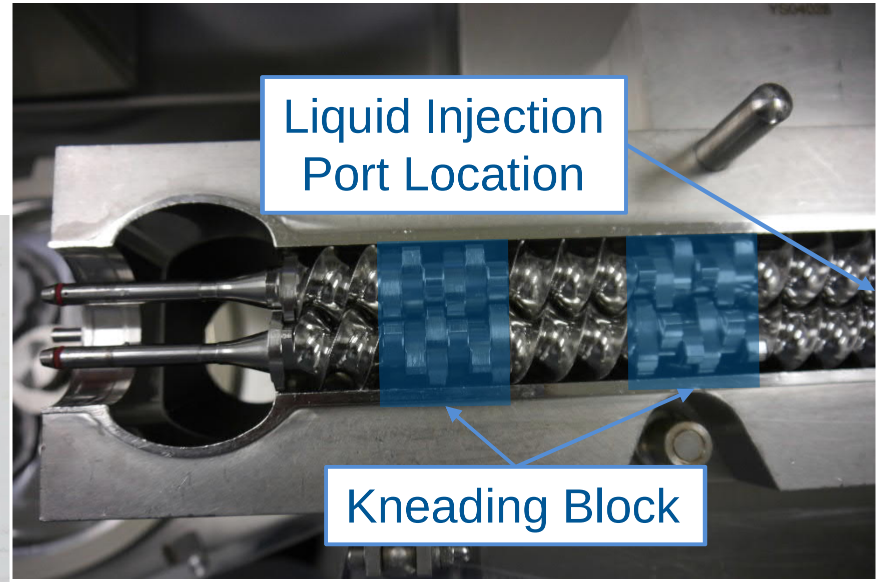
- Generic Framework that can be applied to many different industrial systems



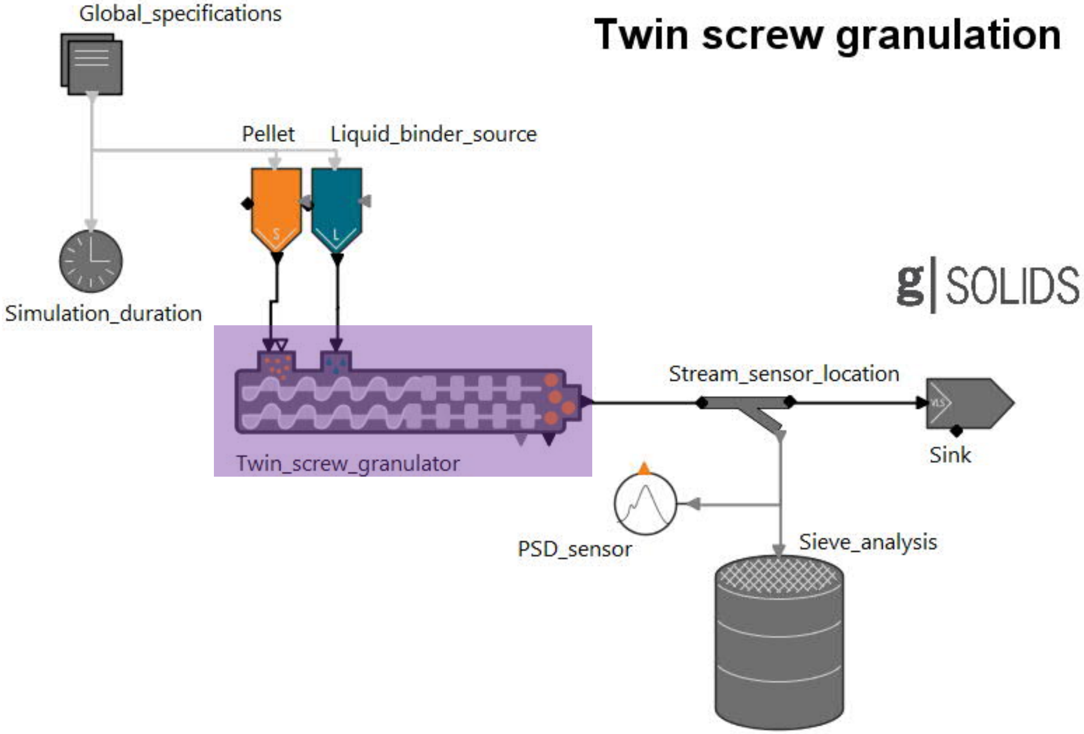


GEA ConsiGma 1 Twin Screw Granulator (TSG)





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:

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

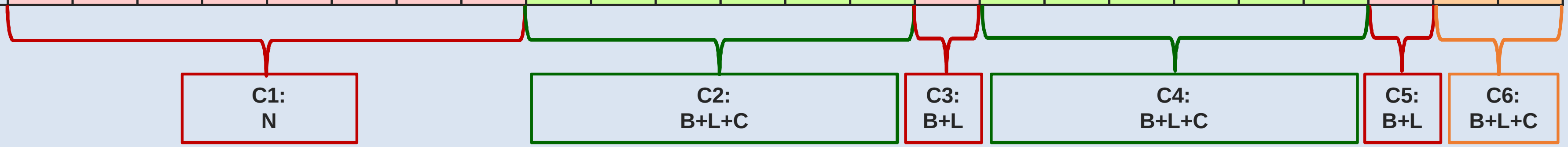
- $n(s,l,g,t)$: population density (a function of particle volume)
- $\frac{\partial}{\partial s}, \frac{\partial}{\partial l}, \frac{\partial}{\partial g}$: state change due to layering, liquid addition and consolidation
- $B_{nuc}(s,l,g,t)$: birth rate due to drop nucleation
- $B_{break}(s,l,g,t)$ and $D_{break}(s,l,g,t)$: birth and death due to breakage
- $\dot{F_{in}}$ and $\dot{F_{out}}$: Inlet and outlet flow rates in the unit

Conceptualisation of TSG in PBM Model - Compartmentalisation

Liquid Injection Point

Flow direction

Element	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Type	C2.0”	C2.0”	C2.0”	C2.0”	C1.5”	C1.5”	C1.0”	C1.0”	K1/4”	K1/4”	K1/4”	K1/4”	K1/4”	K1/4”	C1.5”	K1/4”	K1/4”	K1/4”	K1/4”	K1/4”	K1/4”	C1.5”	K1/6”	K1/6”



Where the kernel B is breakage, C is consolidation, L is layering and N is nucleation

A **compartmental approach** used to evaluate material transport along the granulator and the outlet flow rate is given by:

$$\dot{F}_{out} = \frac{F}{\tau}$$

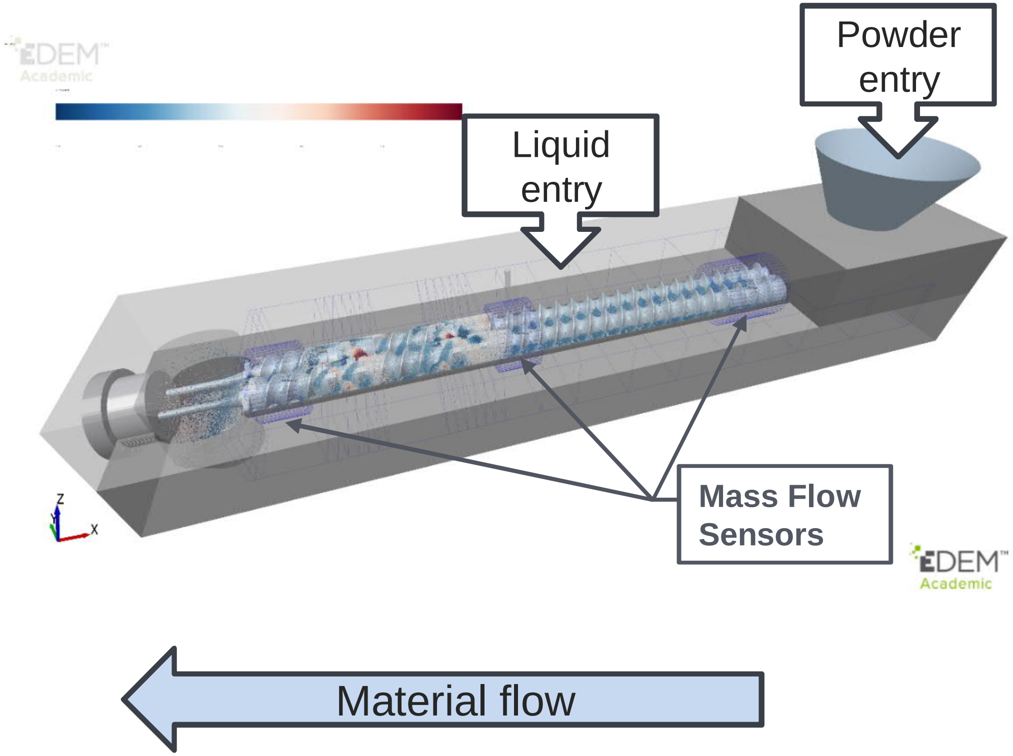
$\dot{F}_{out}$: the outlet flow rate of the unit;
F: mass in the unit;
τ: residence time in the unit

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

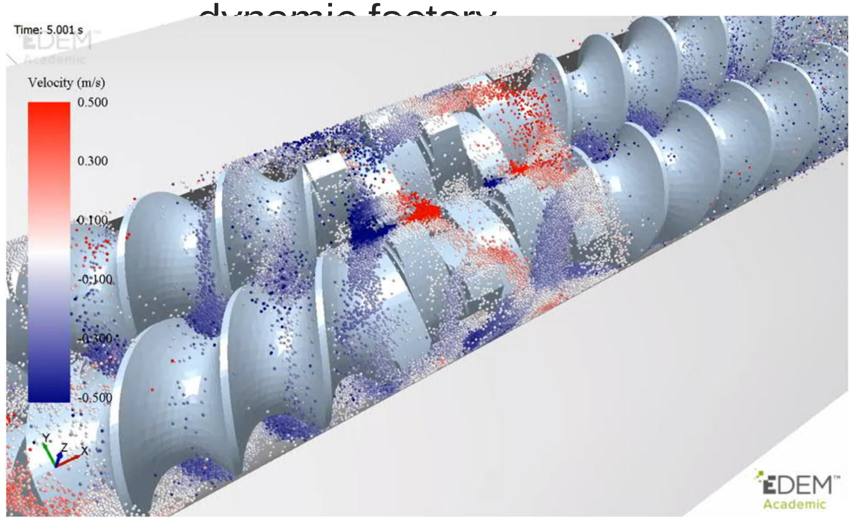
– The residence time τ would be estimated from **DEM** (Barrasso and Ramachandran, 2016)

– **Appropriate kernels** are chosen for each compartment based on **assumed phenomena** in each compartment

Residence Time Estimation from EDEM



- Particle generation by dynamic factory closer to Liquid addition point

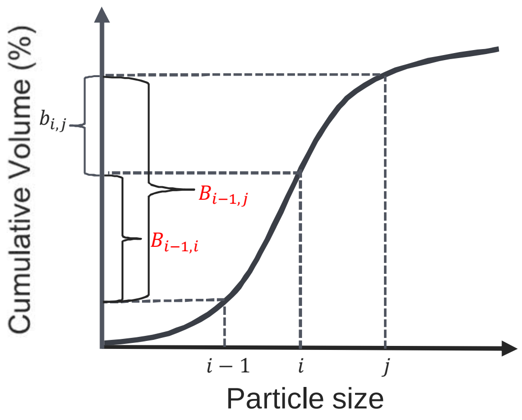


Courtesy by Dr. JP Morrissey from University of Edinburgh

Breakage in PBM

The breakage equation in PBM is given:

$$\frac{dM(i,t)}{dt} = \underbrace{\int_i^\infty S_M(j) b_M(i,j) dj}_{B_{break}} - \underbrace{S_M(i) M(i,t)}_{D_{break}}$$

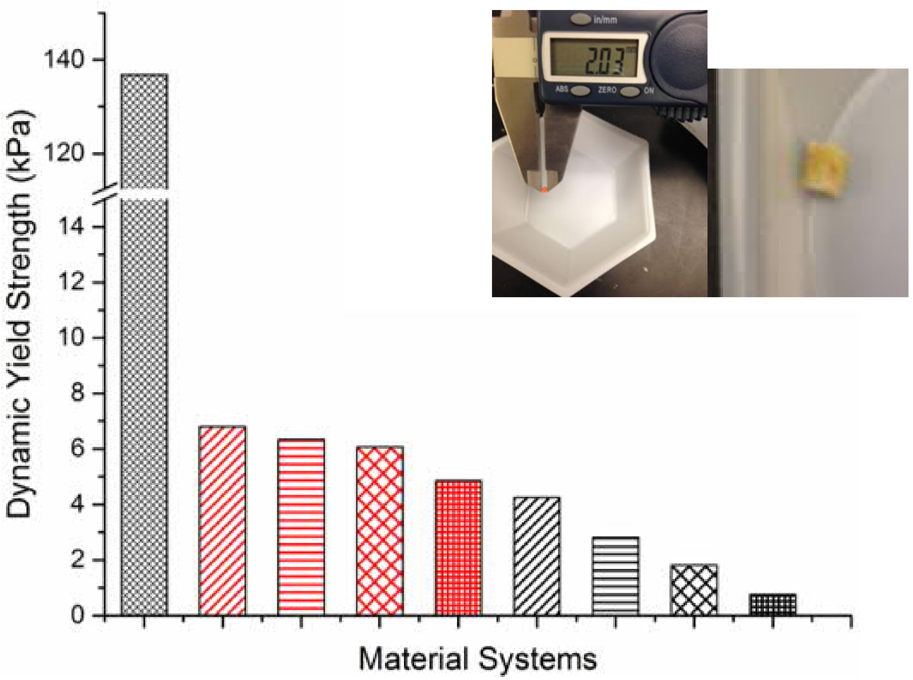


- The selection function S_M and the breakage function $b_M(i,j)$ are the two important functions
- $M(i,t)$: mass of particles with volume i at the time t
- $S_M(i)$ and $S_M(j)$: specific breakage rates of mass fraction of particles of volume i and j
- $b_M(i,j)$: fragment size distribution probability 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

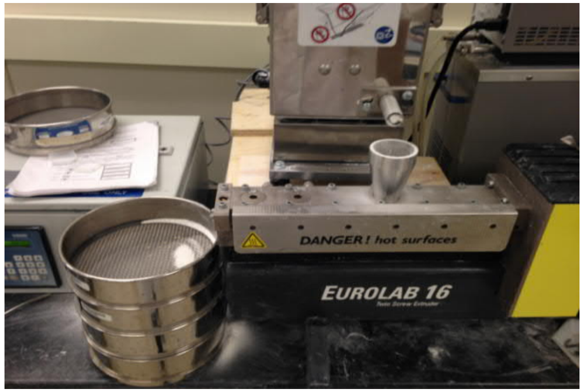
Breakage rate process isolating experiments

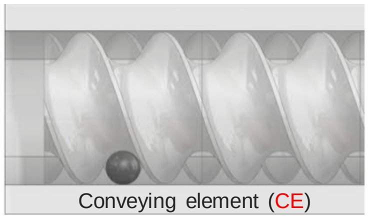


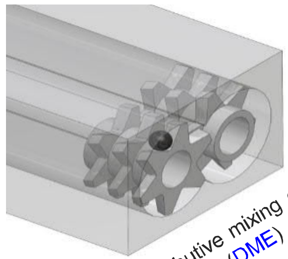
9 different model material systems with two orders of

Magnitude variation in dynamic yield strength

Material Flow

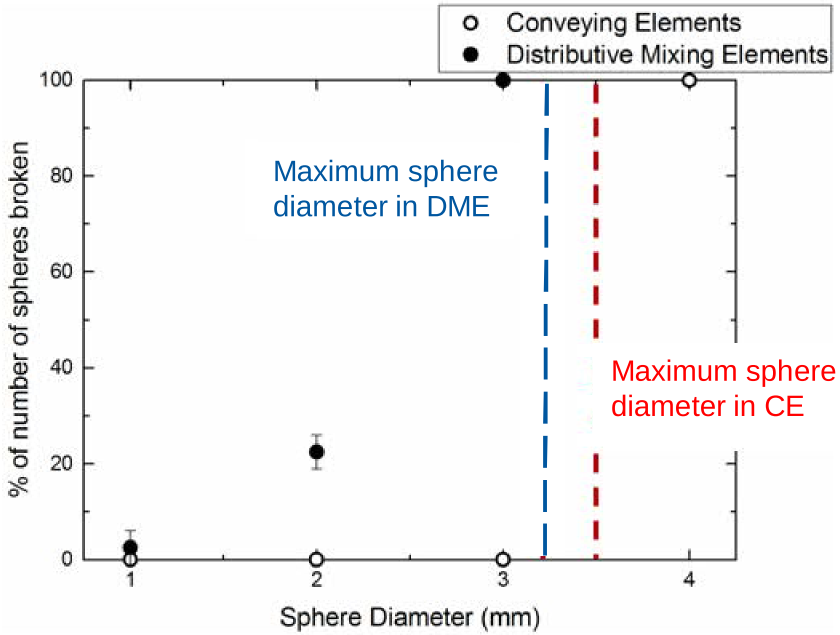






- Breakage characterisation in CE and DMX
- Critical breakage size determined from the geometry gap

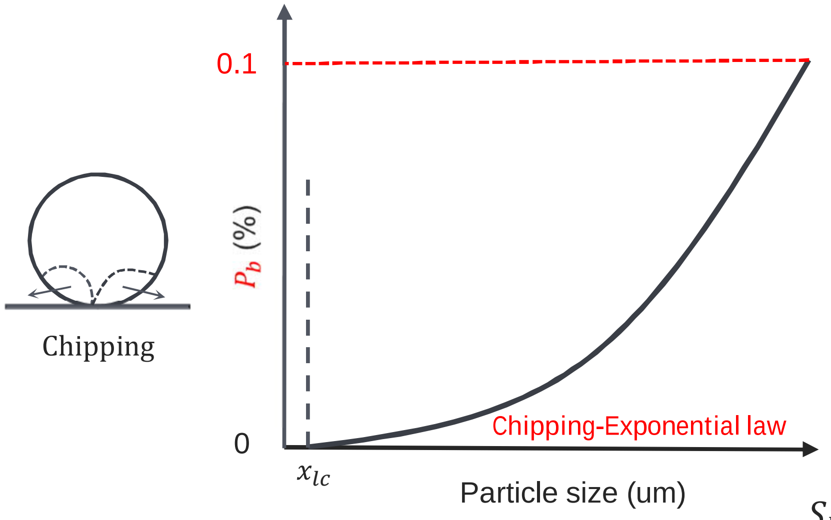
Breakage Test in Screw Elements

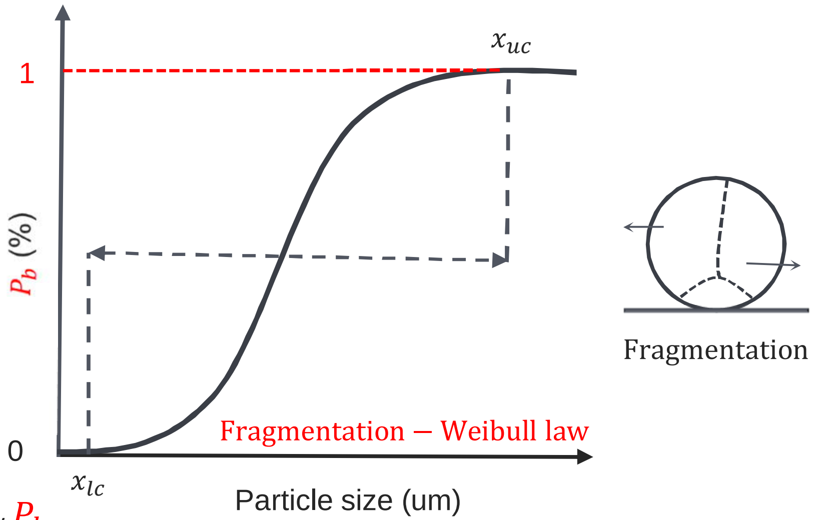


After Pradhan et al. 2017

- 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

Breakage Pattern in TSG



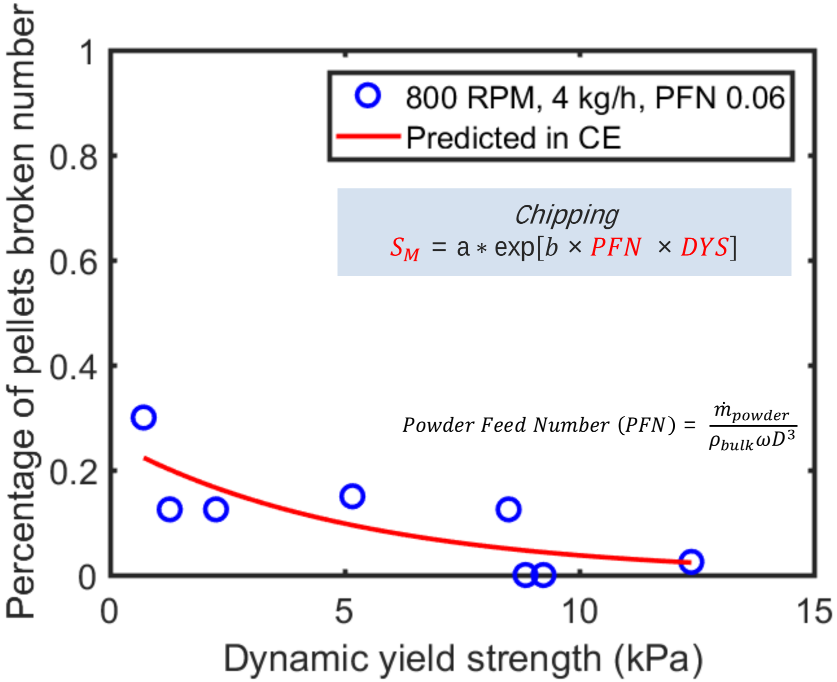


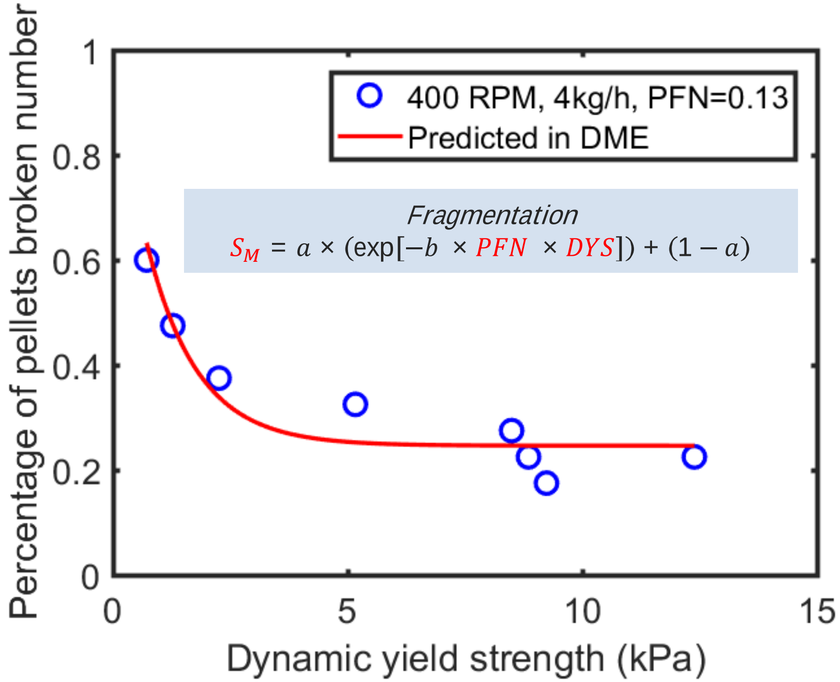
$$S_M = N_{event} P_b$$

- 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

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





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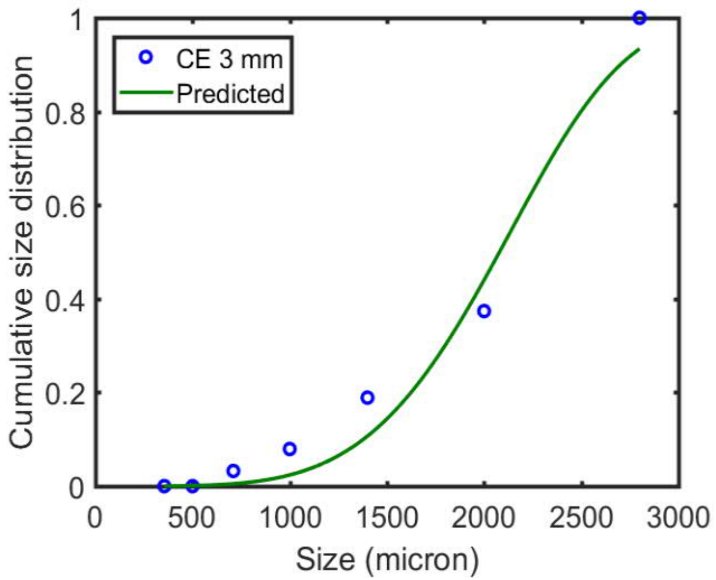
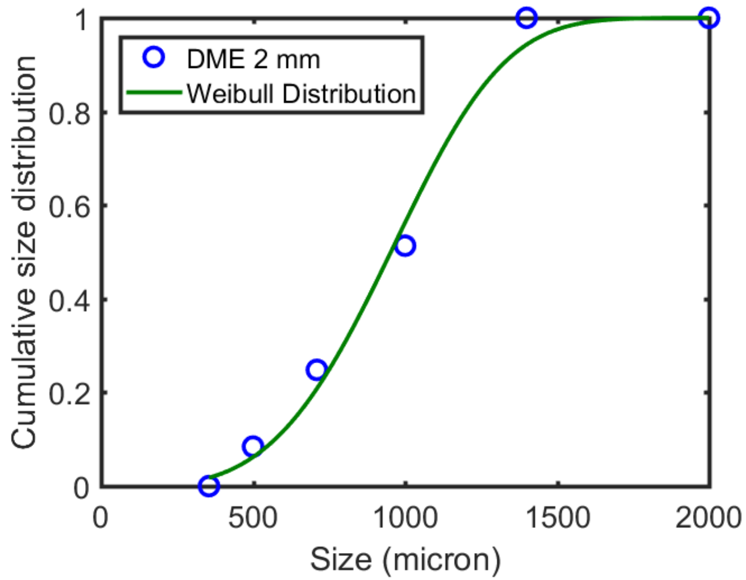
Breakage Function Development in CE and DME





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

$$B_M = \begin{cases} 1 & x > x_{uc} \\ 1 - \exp(-m * (\frac{x}{x_{uc}})^{\wedge}n) & x_{lc} < x < x_{uc} \\ 0 & x < x_{lc} \end{cases}$$

Breakage Kernel

Breakage kernel

Selection function

Conveying element

$$S_M = S_{cM}\begin{cases}1 & x > x_{uc}\\ a * \exp(b * PFN * DYS) * (x/\ x_{lc})\text{^}c & x_{lc} < x < x_{uc}\\ 0 & x < x_{lc}\end{cases}$$

$$S_M = S_{cM}\begin{cases}1 & x > x_{uc}\\ (a * \exp(-b * PFN * DYS) + (1-a)) * (x/\ x_{lc})\text{^}c & \\ 0 & x < x_{lc}\end{cases}$$

Kneading element

Breakage function

$$B_M = \begin{cases}1 & x > x_{uc}\\ 1 - \exp(-m * (\frac{x}{x_{uc}})\text{^}n) & x_{lc} < x < x_{uc}\\ 0 & x < x_{lc}\end{cases}$$

Modified Weibull distribution

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

Modelling Kernel Formation

Rate Processing Kernels

Nucleation

Conveying: addition port

$$D_{m_p,nuc} = \frac{\dot{L}_{in,powder}(x,t)}{V_{droplet}}(1-\epsilon_{bed})V_{nuc}$$

Barrasso and Ramachandran, 2015

Layering

Conveying/Kneading

$$G = G_m \frac{M_{powder}}{kM_{granule} + M_{powder}} exp\, p[-a(x_w - x_{wc})^2]$$

Cameron et al., 2005

Breakage

Conveying/Kneading

$$S_M = \begin{cases} 1 & x > x_{uc} \\ f_n(DYS, PFN, etc.) & x_{lc} < x < x_{uc} \\ 0 & x < x_{lc} \end{cases}$$

Proposed model

$$B_M = \begin{cases} 1 & x > x_{uc} \\ 1 - \exp(-a * (\frac{x}{x_{crit}})\text{^}b) & x_{lc} < x < x_{uc} \\ 0 & x < x_{lc} \end{cases}$$

Modified Weibull distribution

Consolidation

Kneading

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

Iveson et al., 1996

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

Material parameters

PSD: 40-180 um

Shape factor Volumetric = 0.524

Shape factor Surface = 3.141

Etc.

TSG parameters

Conveying1.0 = 25.4 mm

Conveying 1.5 = 38.1 mm

Conveying 2.0 = 50.8 mm

Kneading 1/4 and 1/6 inch

Process parameters

Powder feed rate: 14.4 kg/h

L/S ratio: 0.1-0.3

Mean residence time (CE) = 0.051 s/cm

Mean residence time (KE) = 0.089 s/cm

Breakage function parameters

Weibull distribution

Scale exponent: 2 (6 in CE)

Shape exponent : 2 (6 in CE)

Selection function parameters

Breakage rate constant: 1.3 (2 in KE)

Minimum critical particle size:

1600 µm for conveying

1200 µm for kneading

Maximum critical particle size:

3500 µm for conveying

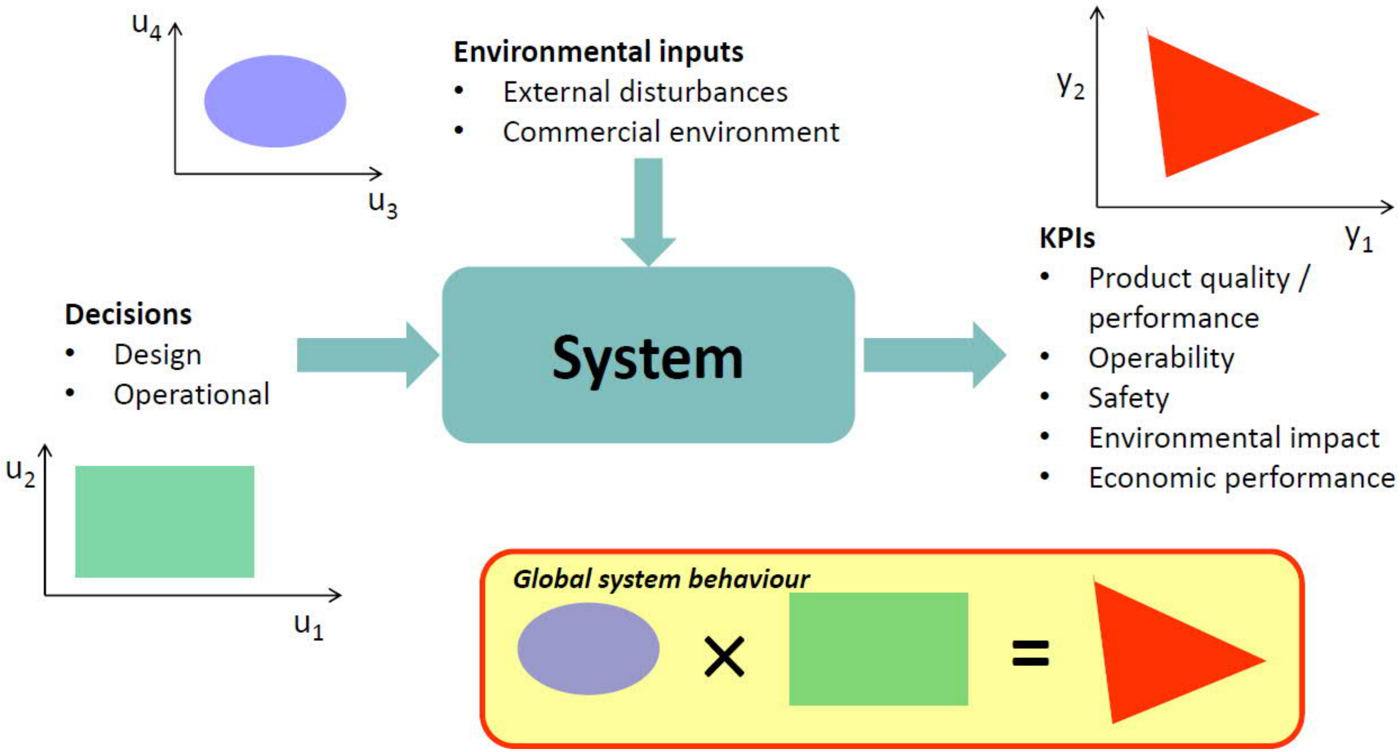
3200 µm for kneading

Size exponent: 1.2

PFN: 0.011

DYS: 10 kPa

Global System Analysis (GSA)



From point calculation to global system analysis (After Costas Pantelides, 2016)
https://www.psenterprise.com/products/gproms/technologies/global-system-analysis

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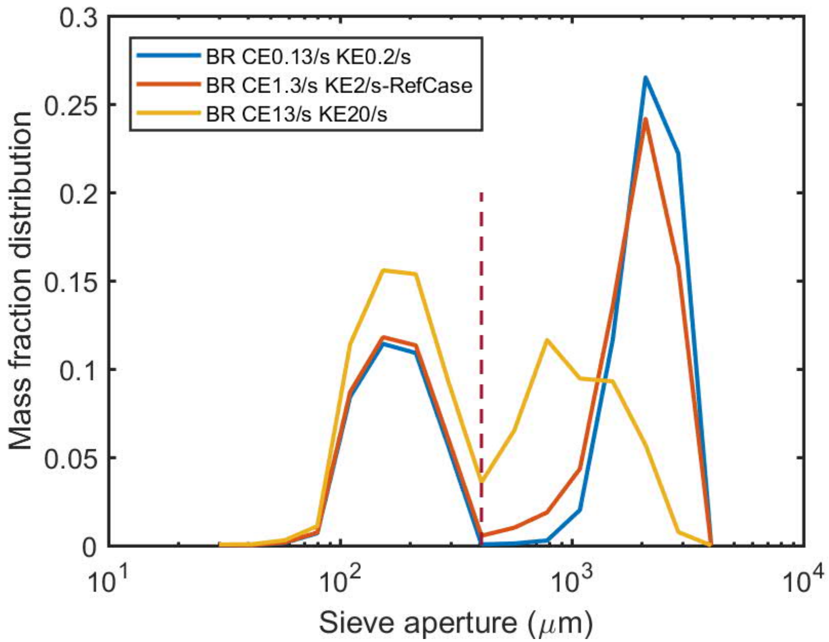
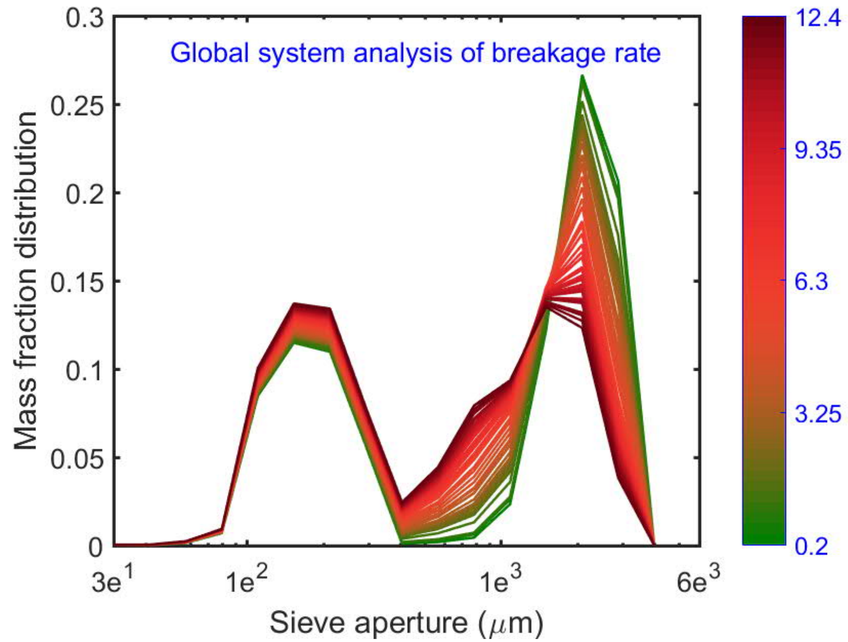
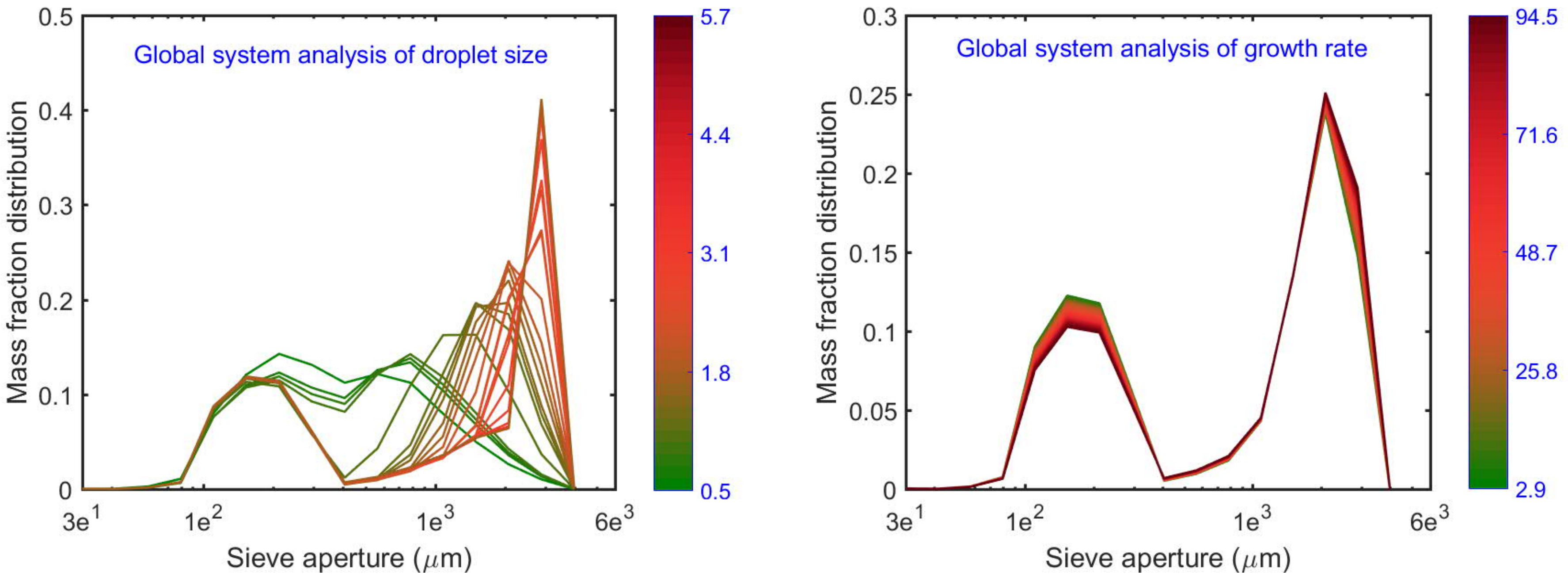
Global System Analysis (GSA)





Discrete point calculation → Global system analysis

Global System Analysis (GSA)



Leverage of PBM Input Parameters using GSA

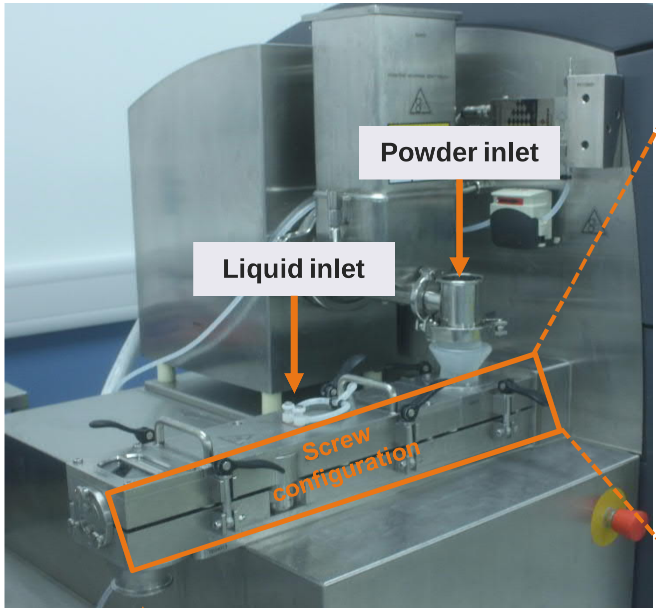
Rate Parameters	Kernel	Influence
Mean droplet size	Nuc.	Large
Nucleus pore saturation	Nuc.	Large
Std of droplet size	Nuc.	Medium
Max growth rate	Layering	Medium
Min moisture content	Layering	Small
Kinetic a	Layering	Small
Kinetic k	Layering	Small

Rate Parameters	Kernel	Influence
Breakage rate	Breakage	Large
Size exponent	Breakage	Large
Min critical size	Breakage	Medium
Max critical size	Breakage	Small
DYS	Breakage	Medium
PFN	Breakage	Medium
Parameter a	Breakage	Medium
Parameter b	Breakage	Medium

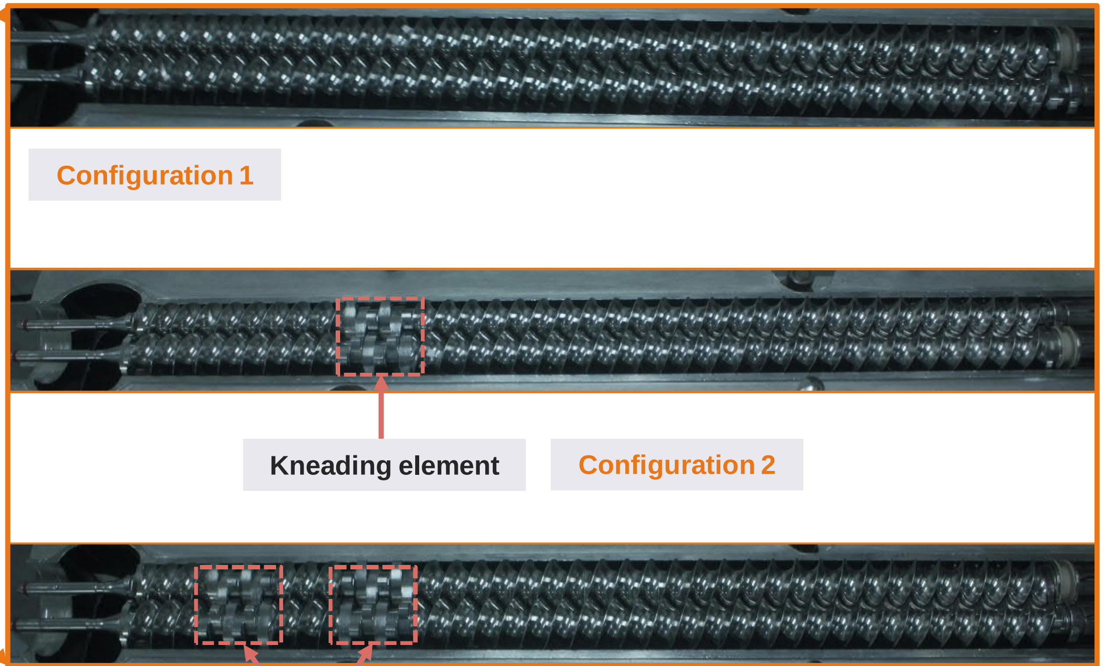
Rate Parameters	Kernel	Influence
Scale m	Breakage	Large
Scale n	Breakage	Large
Cons. rate	Cons.	Small
Minimum porosity	Cons.	Small

Process parameters	Kernel	Influence
L/S ratio	NA	Large
Average RTD	NA	Large

TSG Setup



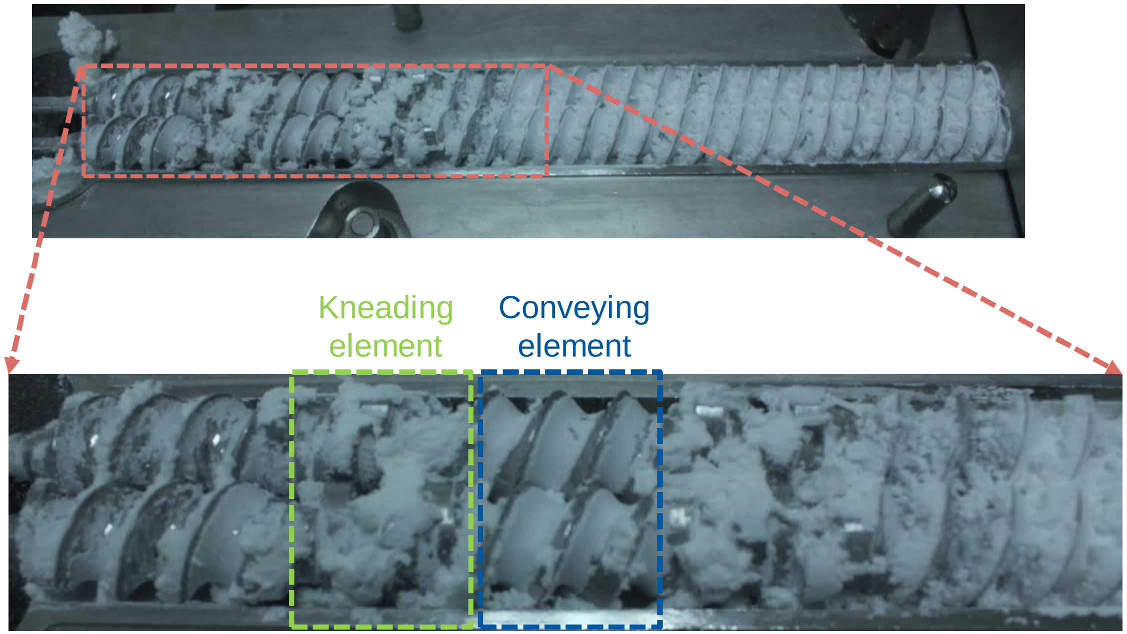
Consigma 25



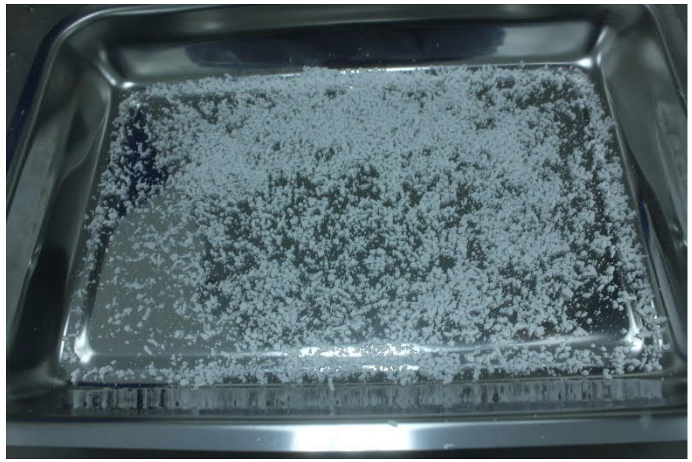
Granulation Test Conducted in AZ

Run	Feed Rate kg/hr	Screw Speed RPM	Screw Configuration	L/S Ratio	Attribute to measure
Group 1 (Calibration)	14	600	C1:CE	0.15 0.25 0.35	GSD Porosity
Group 2 (Calibration)	14	600	C1+KE: 6x60F	0.15 0.25 0.35	GSD Porosity
Group 3 (Validation)	14	600	C1+2KE: 6x60F	0.15 0.25 0.35	GSD Porosity

Observations from DEMC LSR 0.35



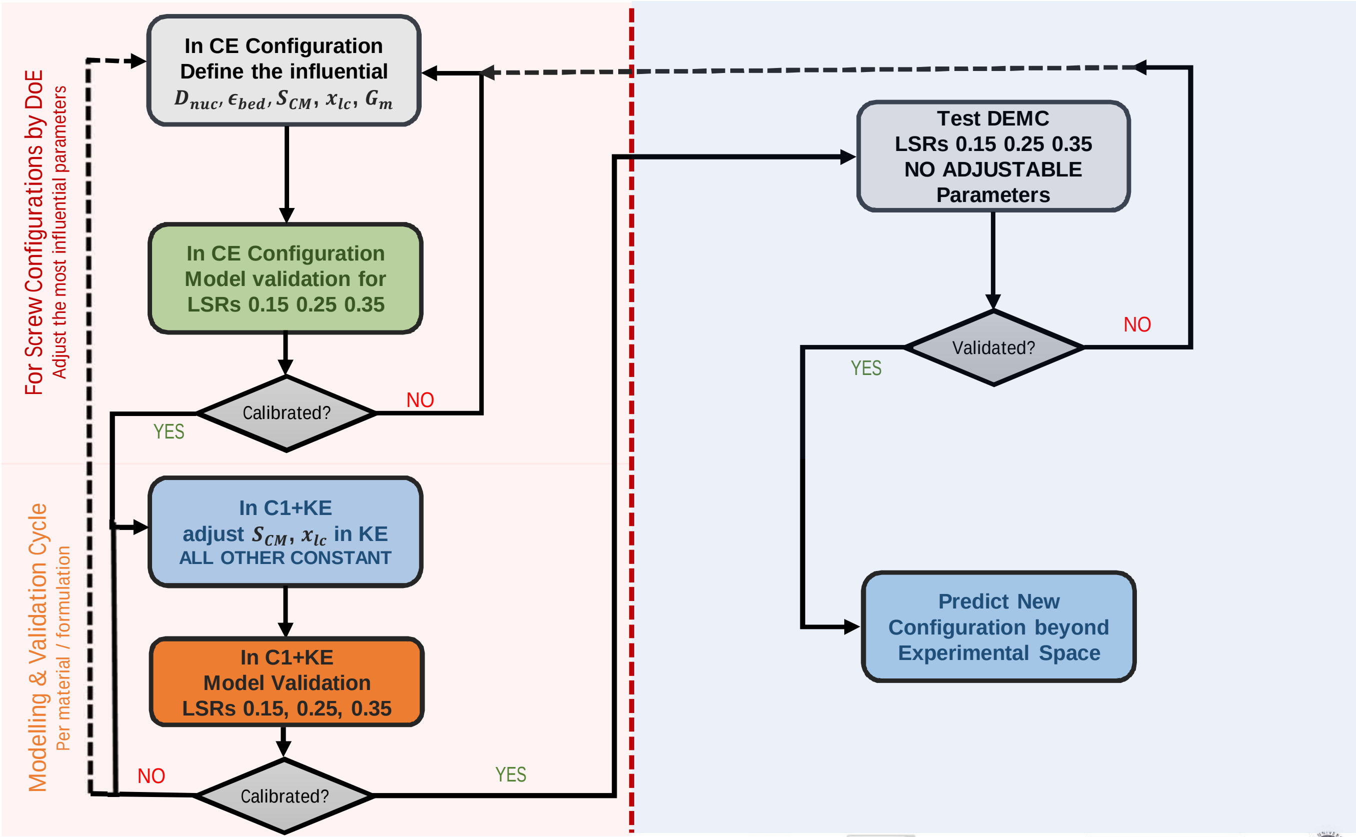
Powder/Paste distribution along the granulator



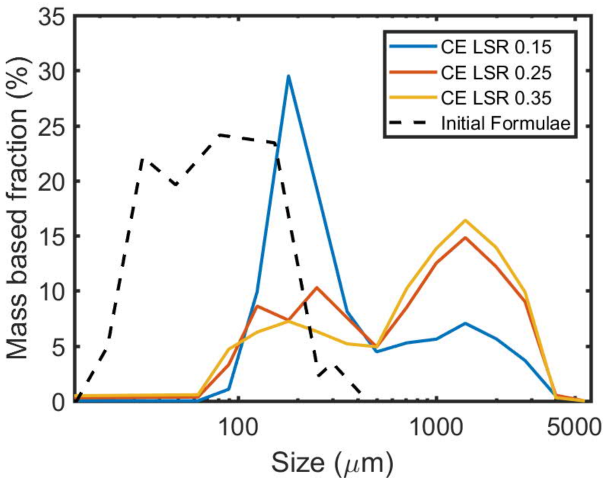
Granule collection pan

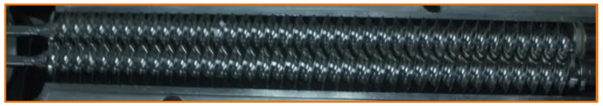
(DEMC LSR 0.35)

Flowchart for PBM Model Validation

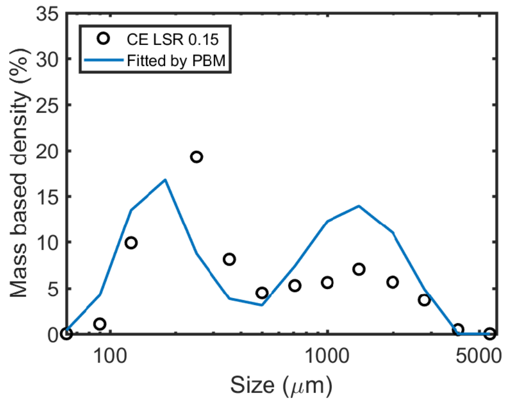


1st Calibration Stage (Conveying Only)

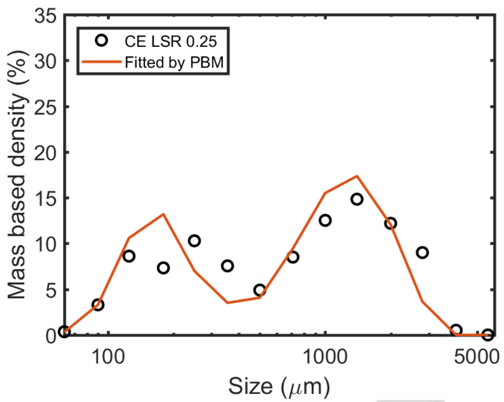


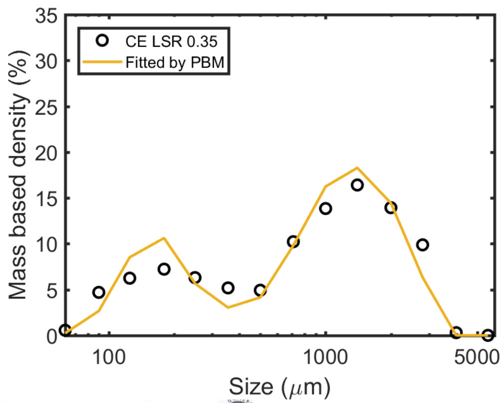


Experimental Result

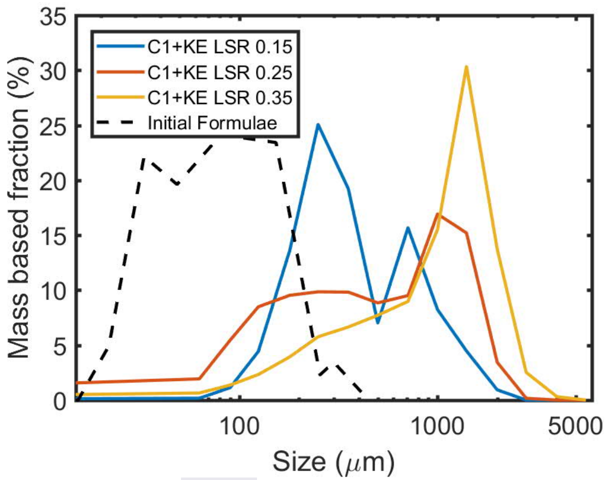


DEM+PBM Calibration Result



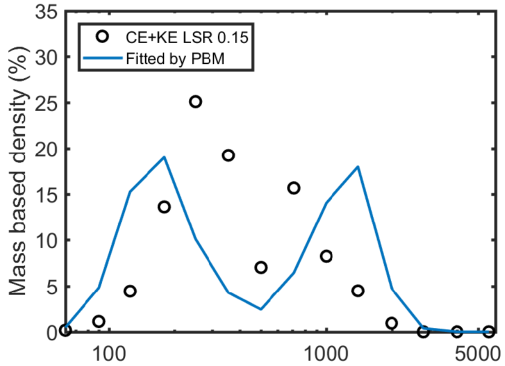


2nd Calibration Stage (Conveying & 1 Kneading Block)

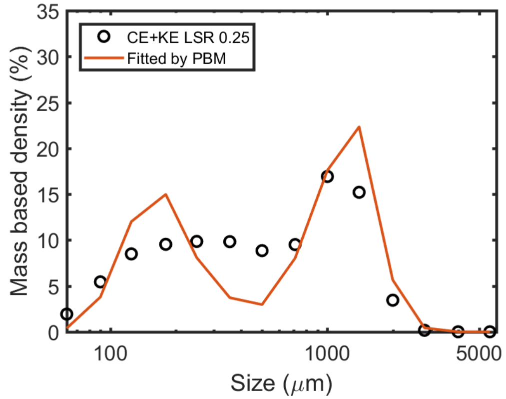


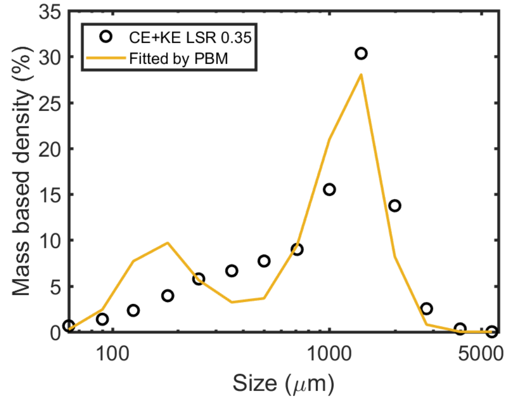
KE

Experimental Result

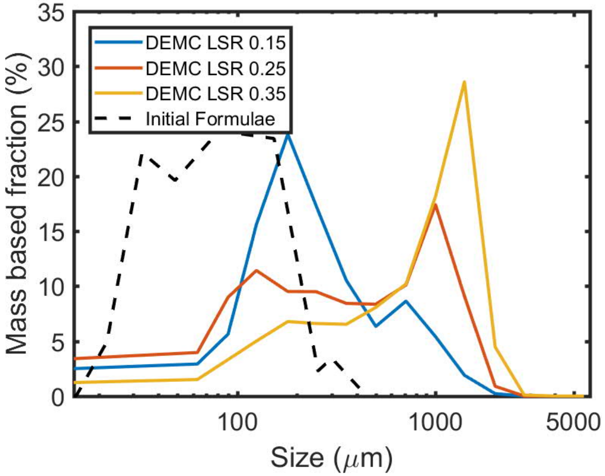


DEM+PBM Calibration Result

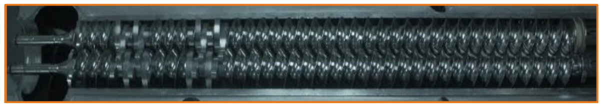




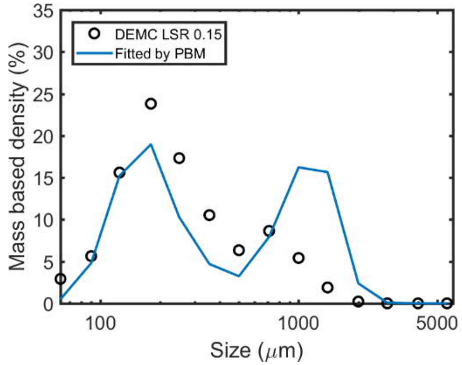
Group 3 - Full Configuration Validation results



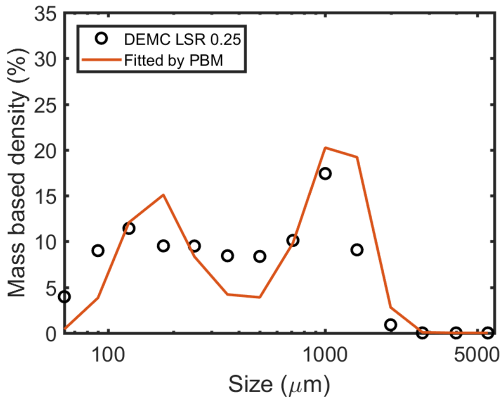
KE KE

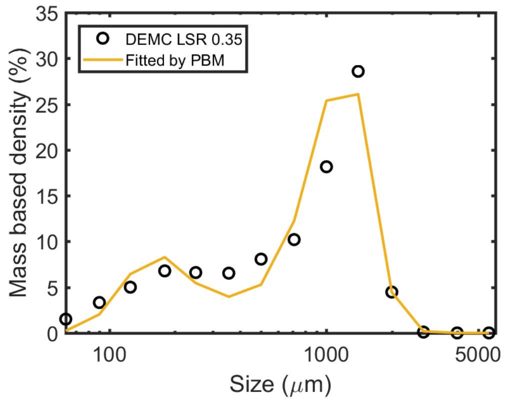


Experimental Result



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!