Understanding Twin Screw Granulation using Global Systems Analysis

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Advanced Process Modelling Forum, London, UK

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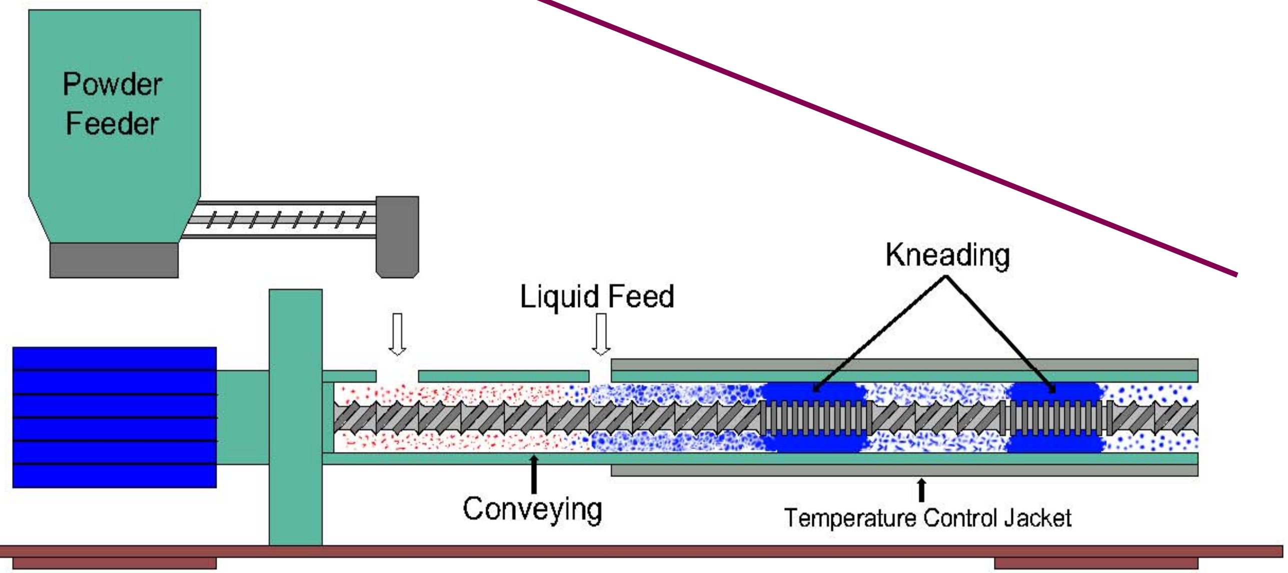
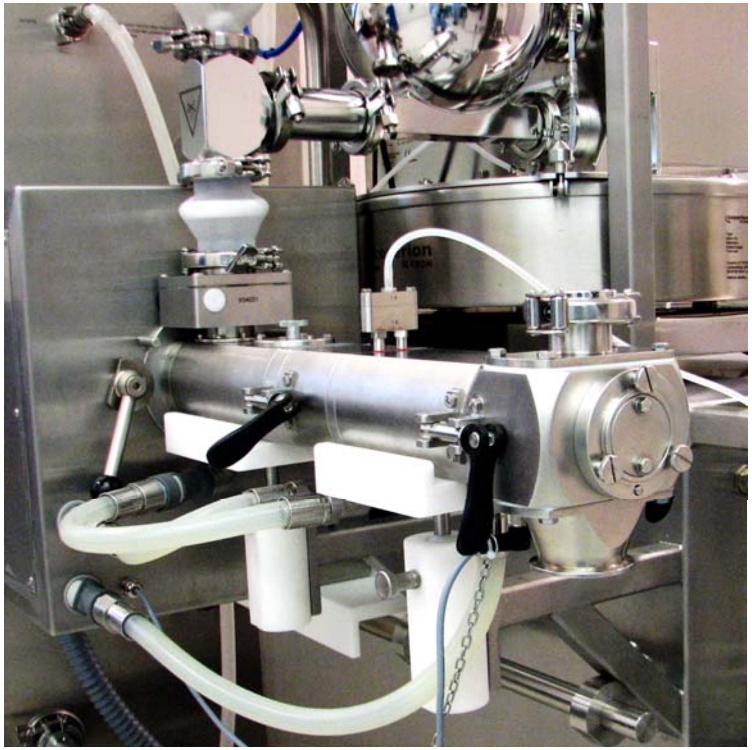
Introduction

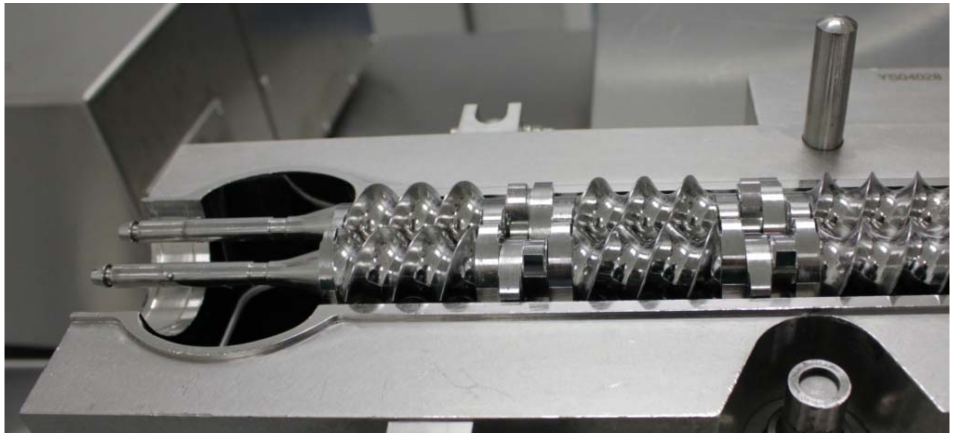
Dispense → Wet Granulate → Dry → Mill → Lubricate → Tablet → Coat

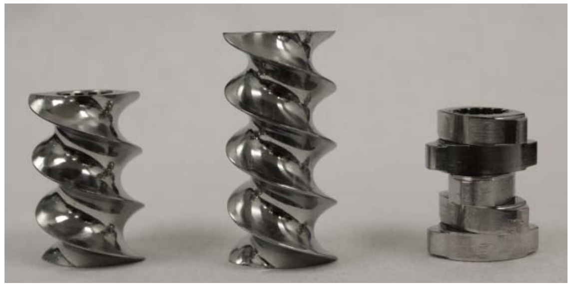


[Seem *et al*. 2015, *Pow Tech* 276]

Introduction





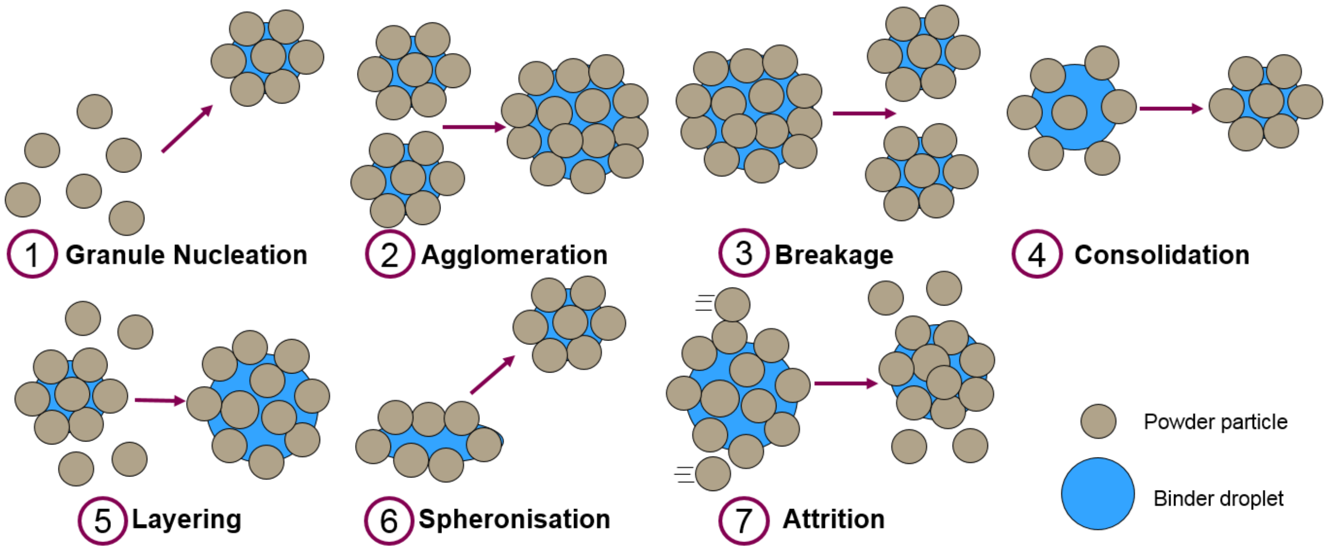


- Highly configurable screw layout
- Main process parameters
  - Powder feed rate
  - Liquid feed rate
  - Screw speed

Finding an optimal design and operational space for a new formulation can consume significant time and material

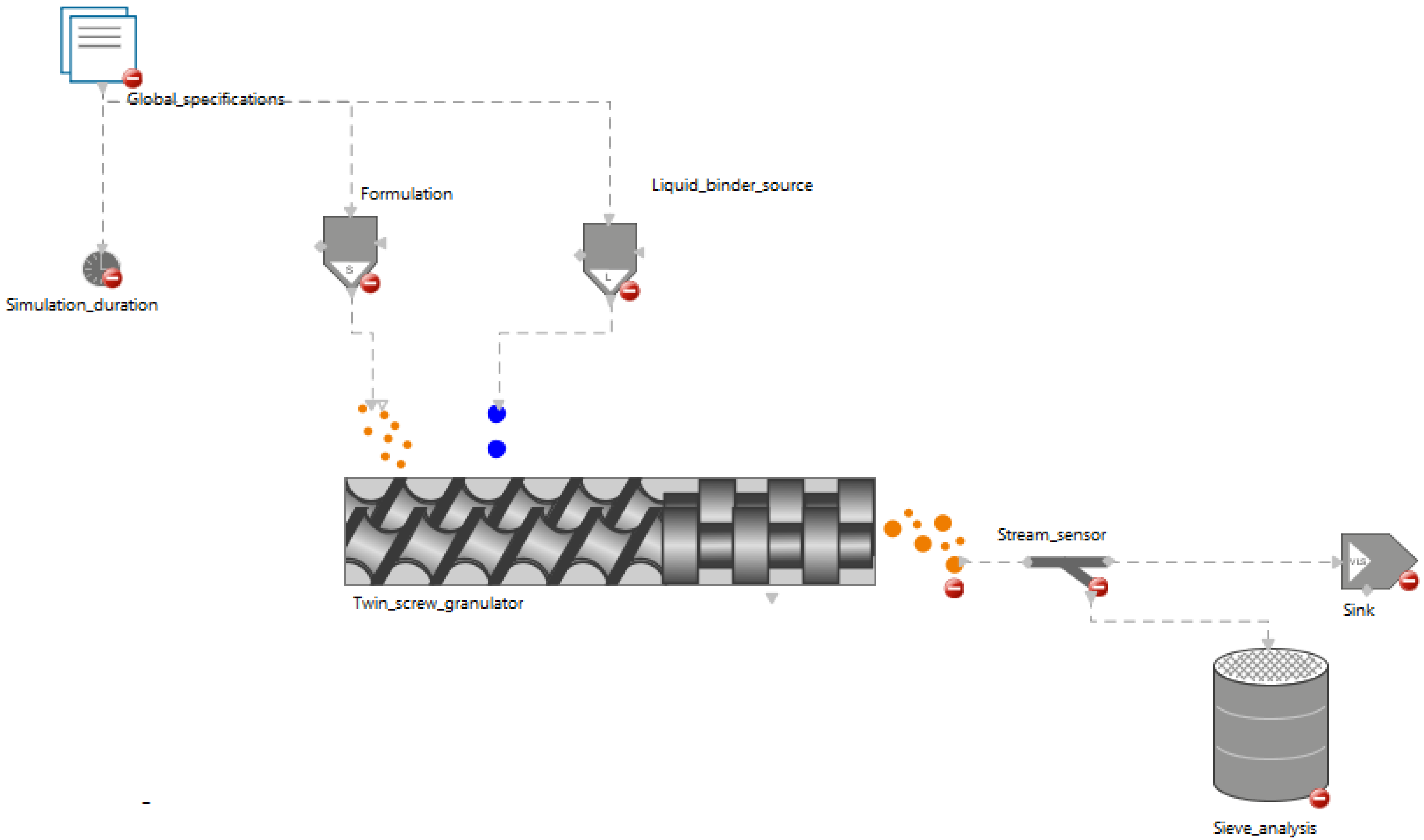
Can modelling make this more efficient?

Introduction



- Many rate processes occur simultaneously during the granulation process
- Population balance modelling can be used to model the changing properties of the granules as a result of these rate processes
- gFormulate has a model for a twin screw granulator

gFormulate


Global_specifications
Formulation
Liquid_binder_source
Simulation_duration
Twin_screw_granulator
Stream_sensor
Sink
Sieve_analysis

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TSG Compartmental Model Overview

Screw Configuration

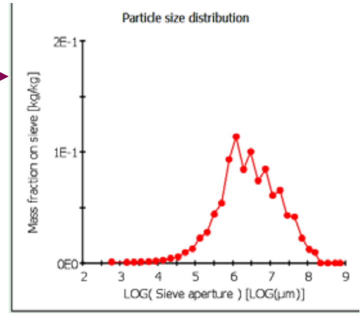
Mechanism Parameters

Mechanism Rates

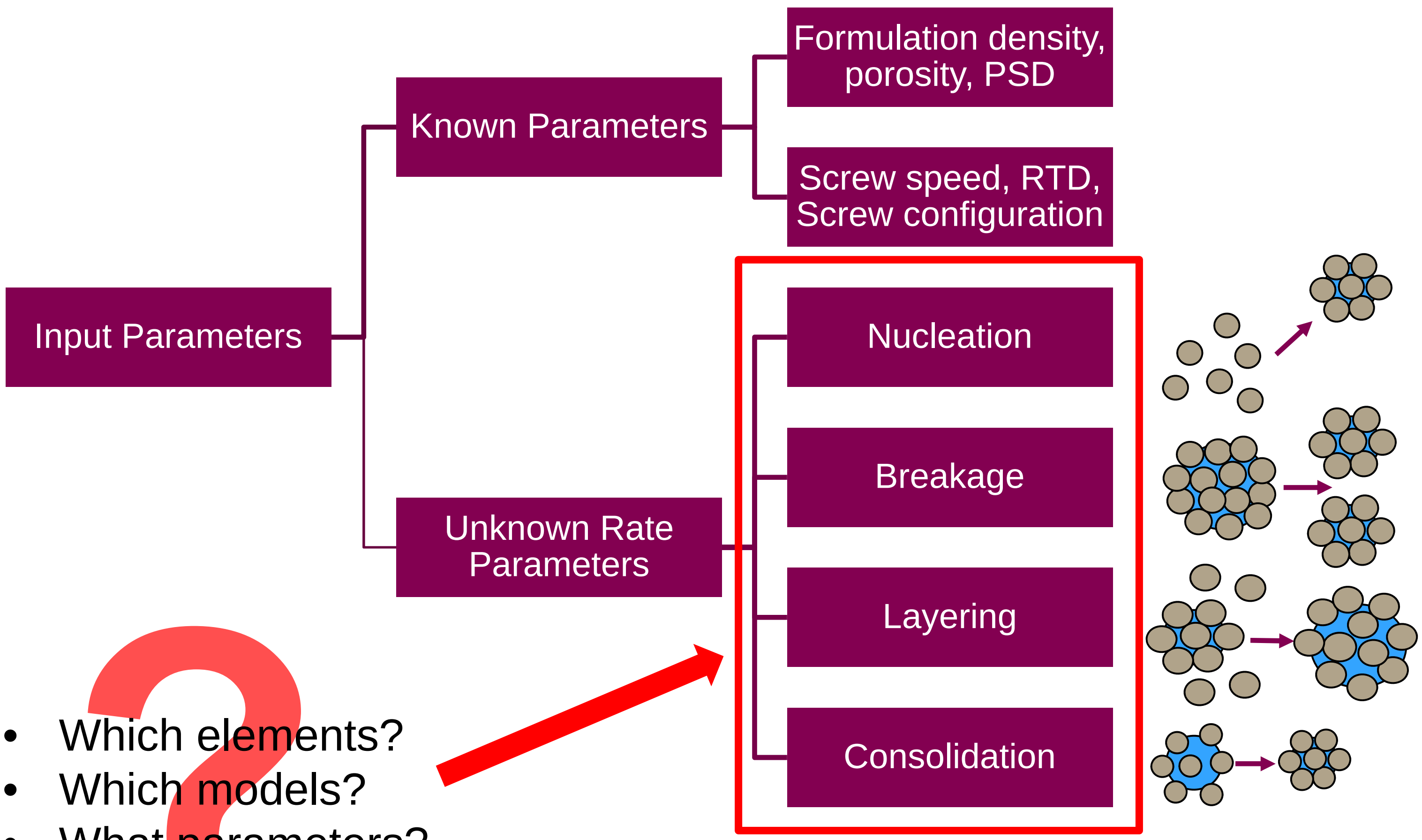
Formulation Properties (Density, Porosity, PSD)

PSD Previous Element

Equipment Parameters (L/S ratio, residence time)



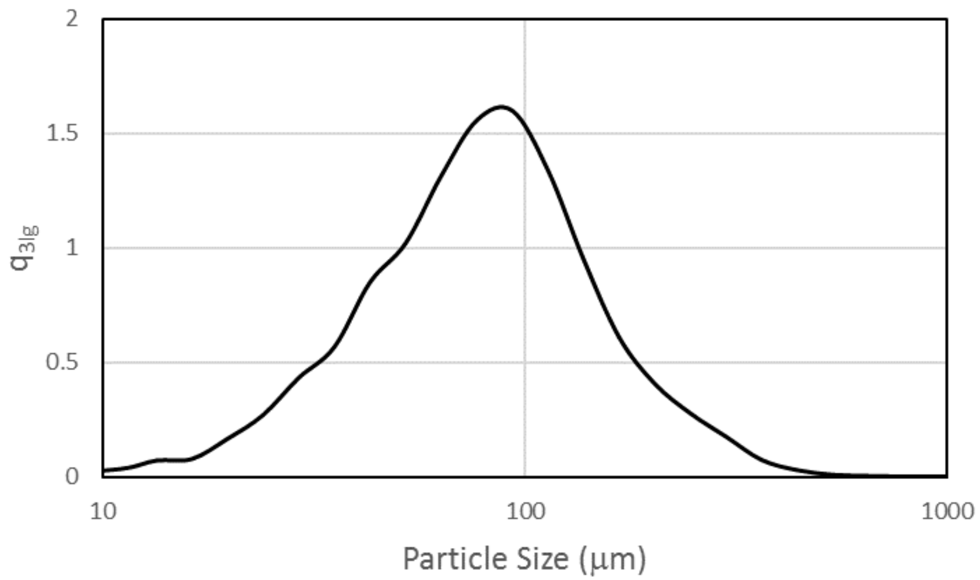
TSG Model Input Parameters



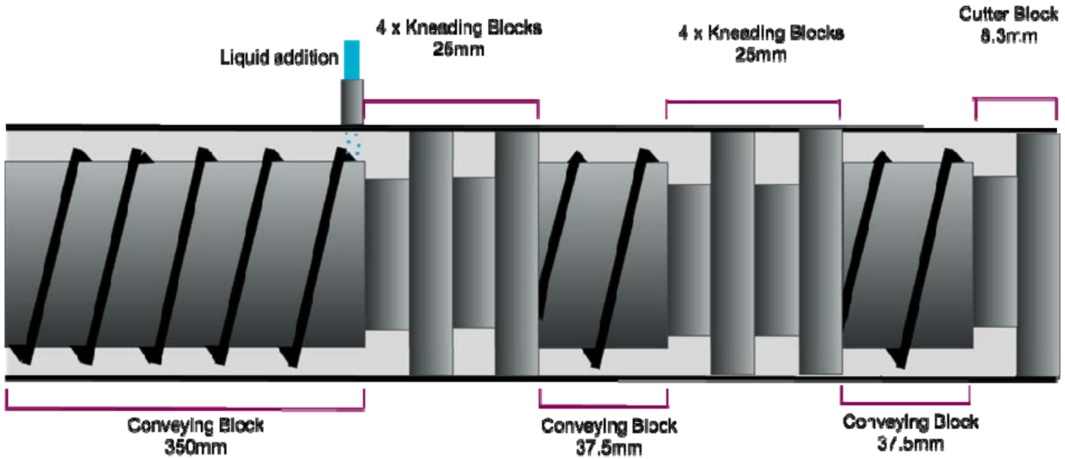
- Which elements?
- Which models?
- What parameters?
- What rates?

Reducing the complexity – what do we know?

- Formulation properties
  - Density
  - Packing fraction
  - Particle Size Distribution
- Process parameters
  - Powder feed rate
  - Water feed rate
  - *Screw speed*

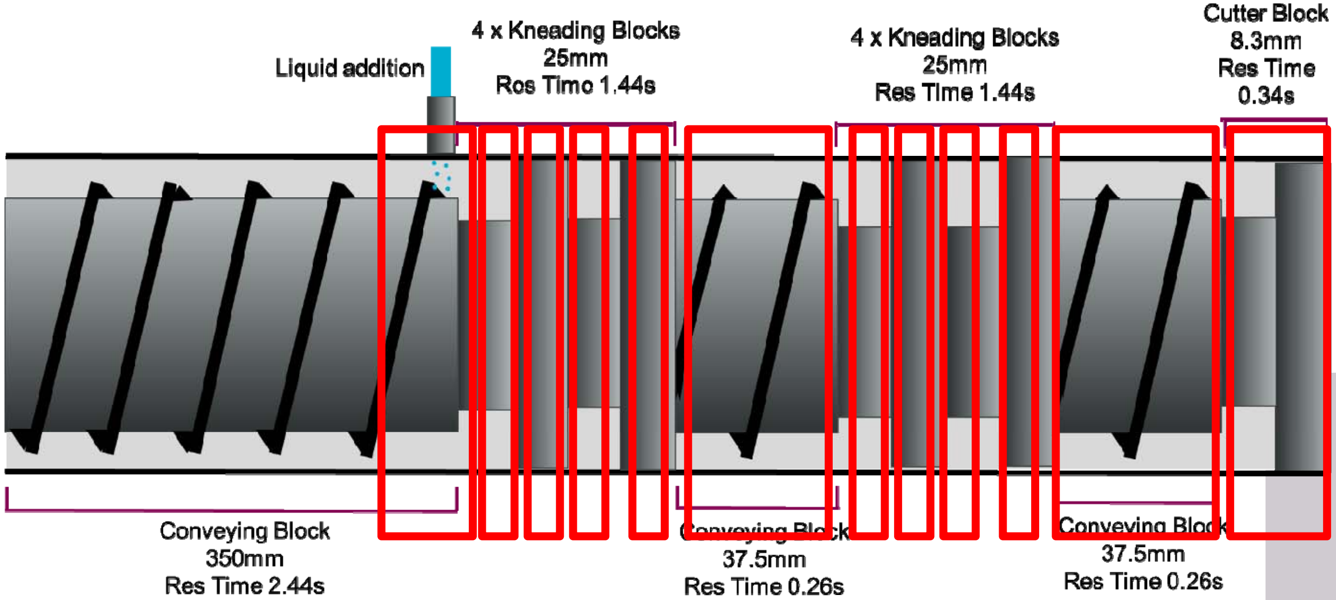


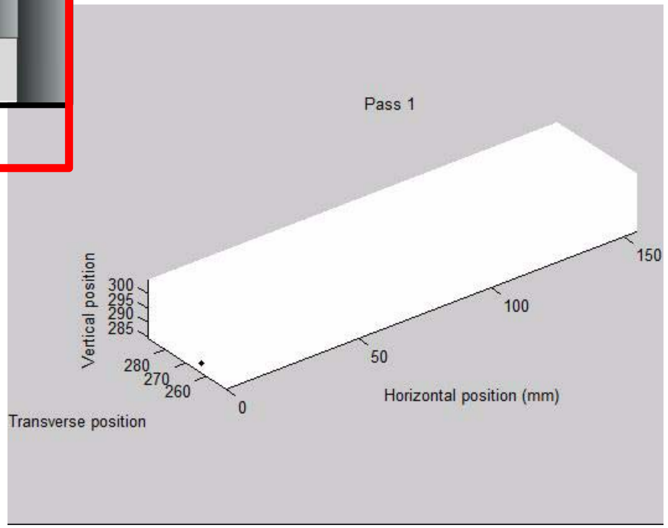
- Screw configuration



Reducing the complexity – what can we estimate?

- Simplify number of compartments (blocks rather than each element)





[Seem *et al*. 2016, *Eur. J. Pharm. Biopharm.* 106]

- Residence time distribution
  - Significantly longer in kneading sections
  - Estimated from published graphs
    - Kumar *et al.* 2014 *Eur. J. Pharm. Biopharm.* 87

Unknown rate parameters

Unknown Rate Parameters

Nucleation

2 Unknowns

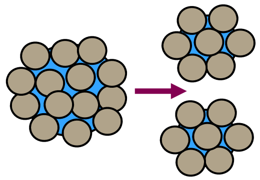
Droplet size

Droplet pore penetration

Breakage

3 Unknowns

Kneading/Cutting



$$S_M = \begin{cases} Sc_M \left(\frac{y}{y_c}\right)^{\alpha} & \text{for } y \geq y_c \\ 0 & \text{for } y < y_c \end{cases}$$

Breakage Rate Constant

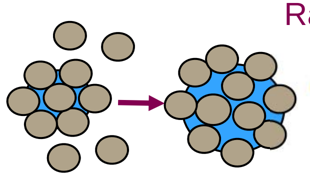
Alpha

Critical Particle Size

Layering

4 Unknowns

All elements



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

Max Growth Rate

Kinetic A

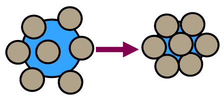
Kinetic K

Minimum Moisture Content

Consolidation

2 Unknowns

Kneading/Cutting



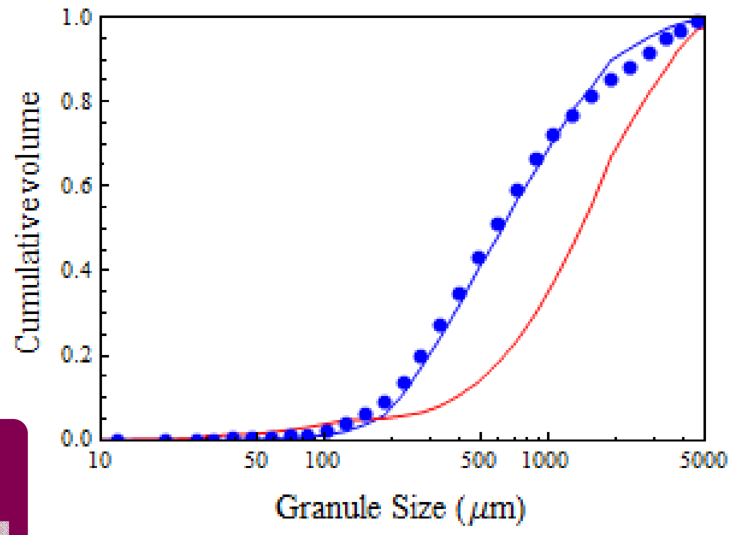
$$\frac{d\varepsilon}{dt} = -k(\varepsilon - \varepsilon_{min})$$

Consolidation Rate Constant

Minimum porosity

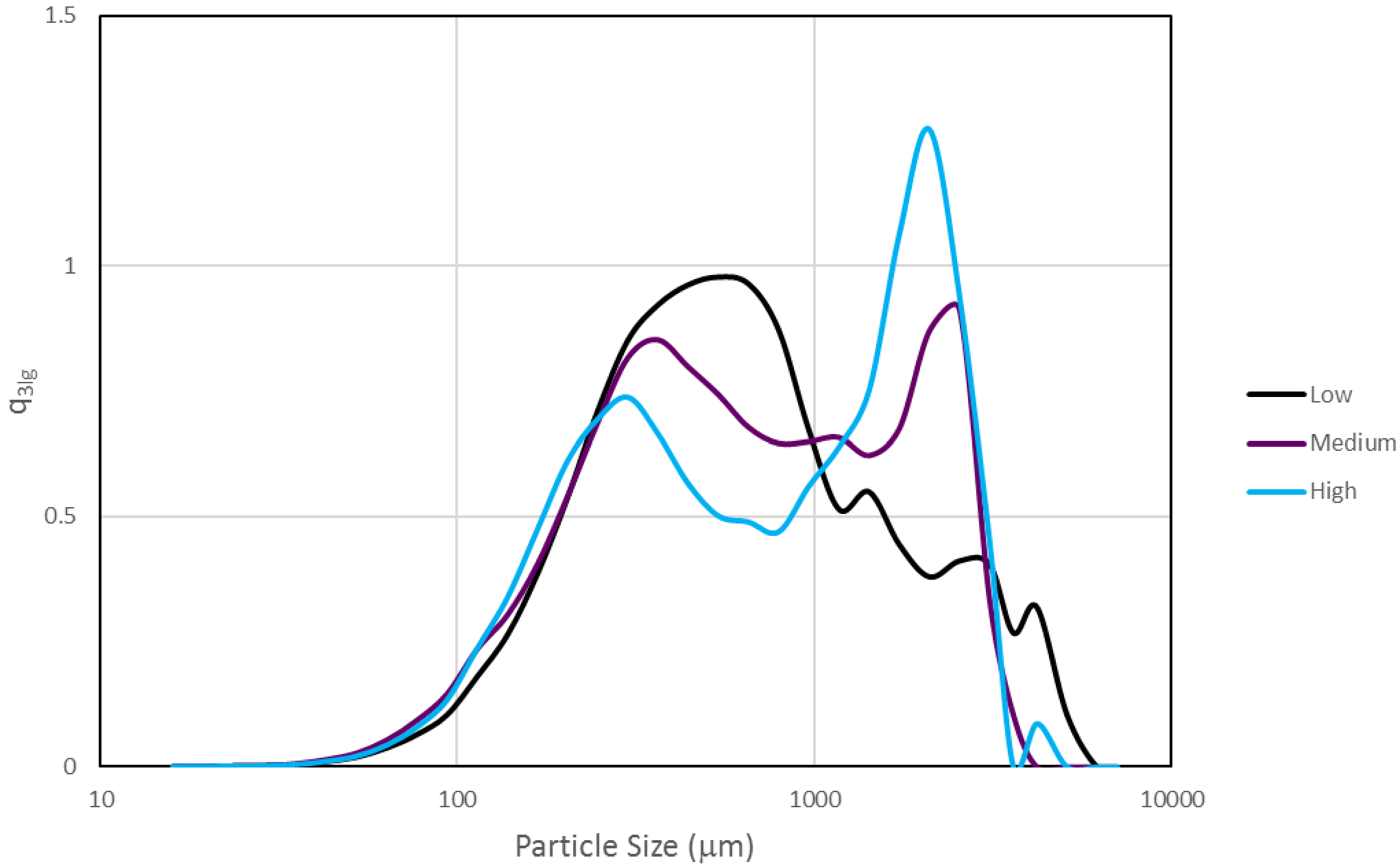
Methodology to estimate rate parameters

- Utilise global systems analysis (GSA) to automatically interrogate model across parameter space
- Calculate a square error (SSE) of the granule size distribution with measured data



- All parameters, large range
- Identify feasible region for each parameter – Graphical Comparison and SSE
- Eliminate less significant variables
- 5 parameters (3 breakage, 2 layering), small range
- Find parameter sets that minimise SSE

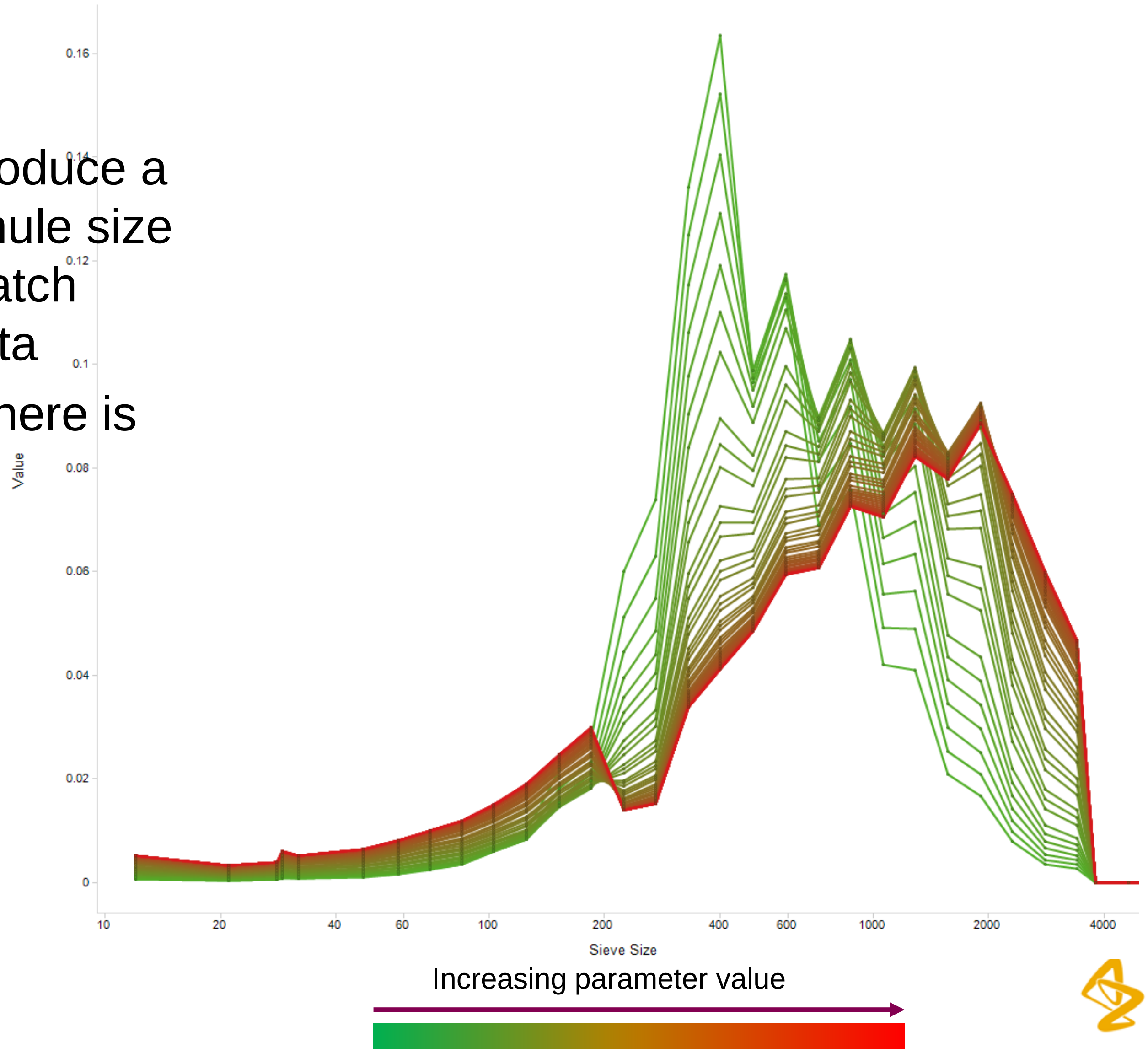
Experimental Granule Size Distribution



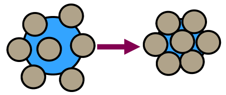
- Increasing proportion of large granules when moving from low to high granulating water amount.

Eliminating Parameters – Nucleation

- **Drop size**
  - Lower values produce a peak at low granule size that does not match experimental data
  - Above 1.5 mm there is little to no effect



Eliminating parameters – Consolidation

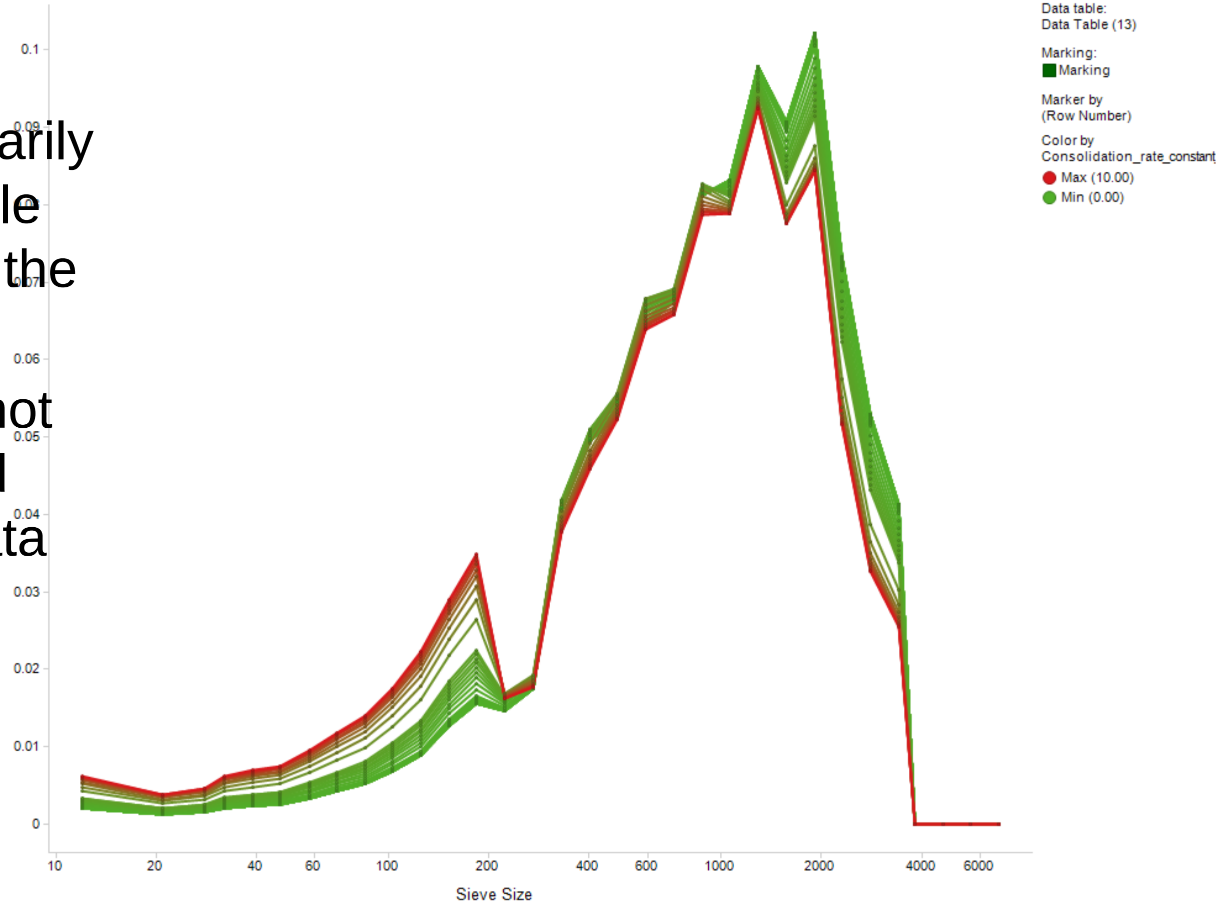


$$\frac{d\varepsilon}{dt} = \boxed{-k}(\varepsilon - \boxed{\varepsilon_{min}})$$

Consolidation Rate Constant

Minimum porosity

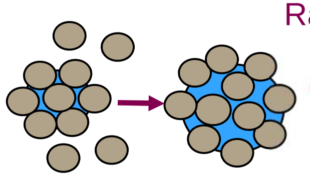
- **Consolidation rate**
  - Very little effect
  - This parameter primarily influences the granule porosity, rather than the granule size
  - This parameter cannot be directly estimated from granule size data



Increasing parameter value

Eliminating parameters – Layering

Increasing parameter value



Max Growth Rate

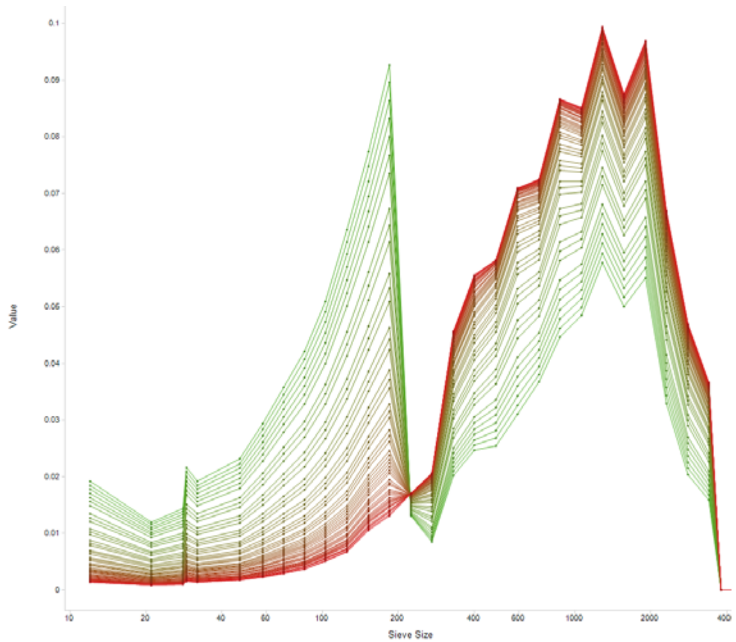
Kinetic A

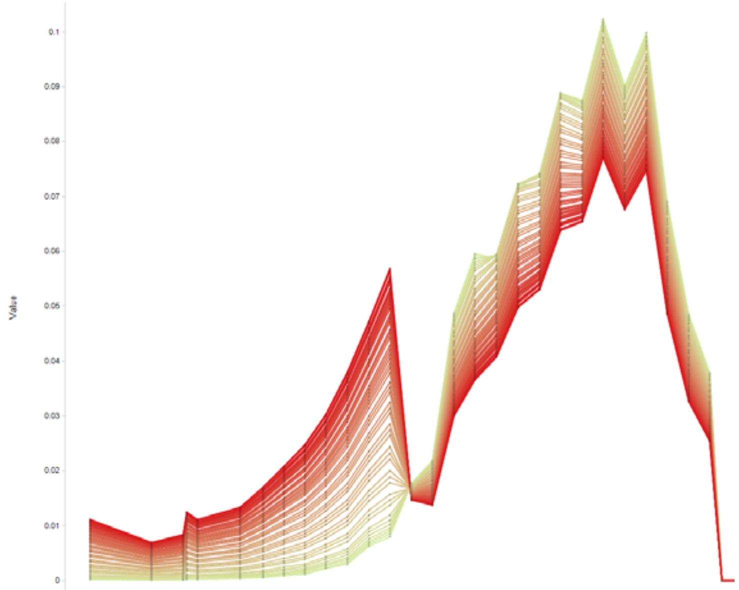
$$G = G_m \frac{M_{powder}}{kM_{granulate} + M_{powder}} \exp[-a(x_w - x_{wc})^2]$$

Kinetic K

Minimum Moisture Content

- **Max Growth Rate**
  - Low values give an unusual bimodal distribution

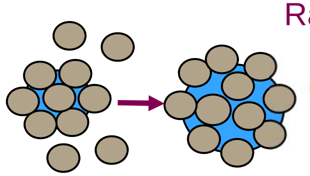




- **Kinetic K**
  - High values give an unusual bimodal distribution

Eliminating parameters – Layering

Increasing parameter value



Max Growth Rate

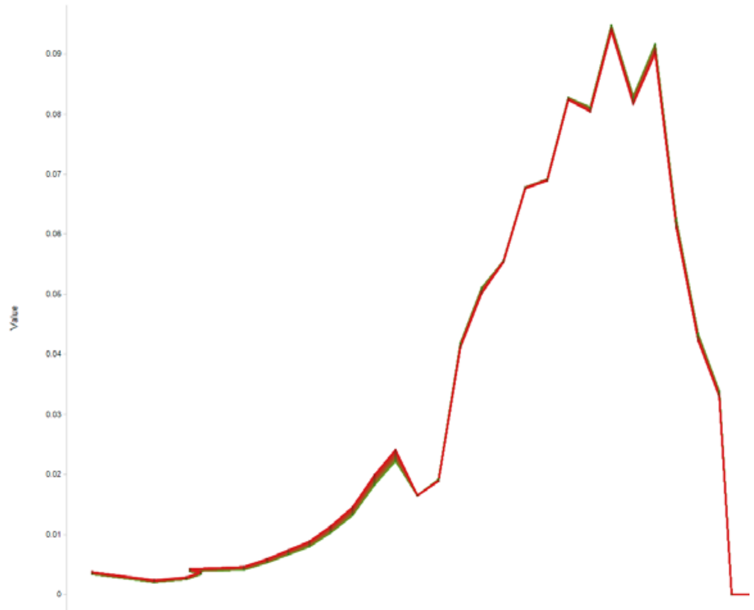
Kinetic A

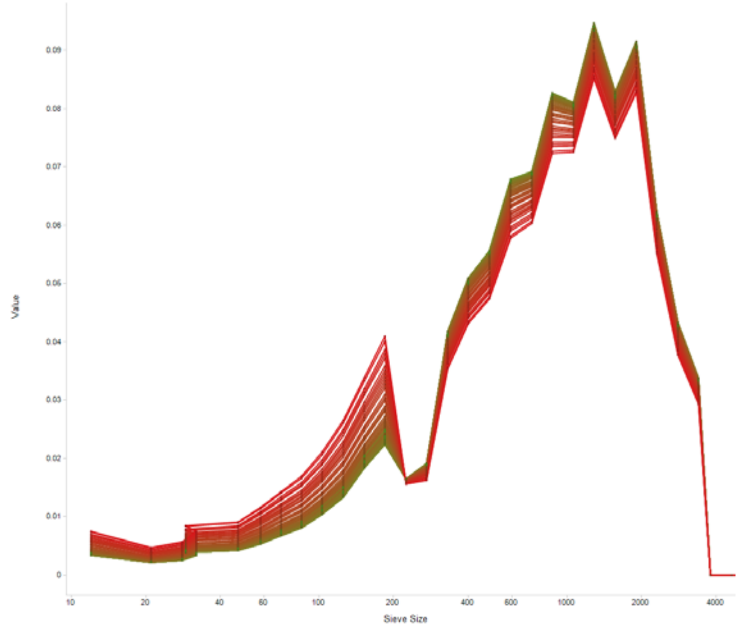
$$G = G_m \frac{M_{powder}}{kM_{granulate} + M_{powder}} \exp[-a(x_w - x_{wc})^2]$$

Kinetic K

Minimum Moisture Content

- **Kinetic A**
  - Little effect



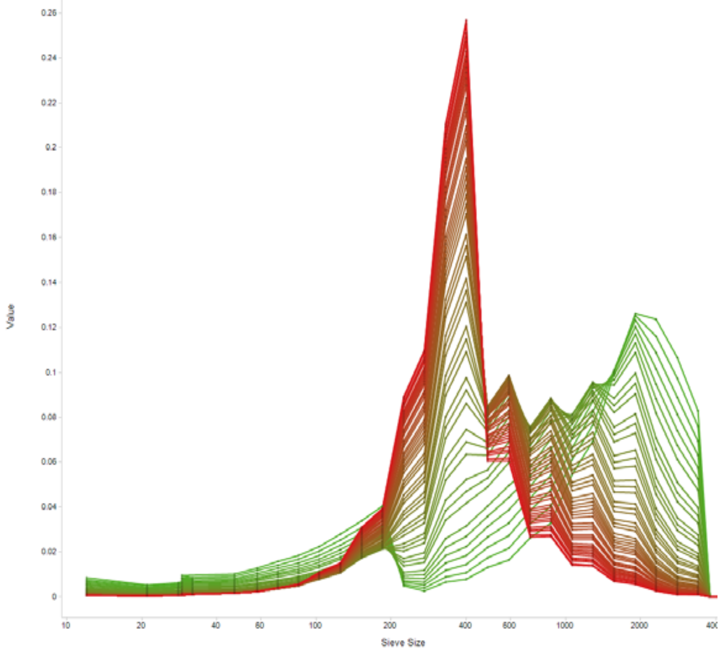


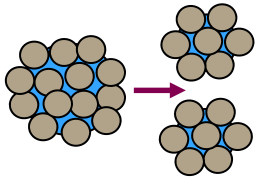
- **Min moisture content**
  - Little effect except at very high values

Eliminating parameters – Breakage

Increasing parameter value

- **Breakage rate constant**
  - Significant effect
  - Low values give unrealistically large granules



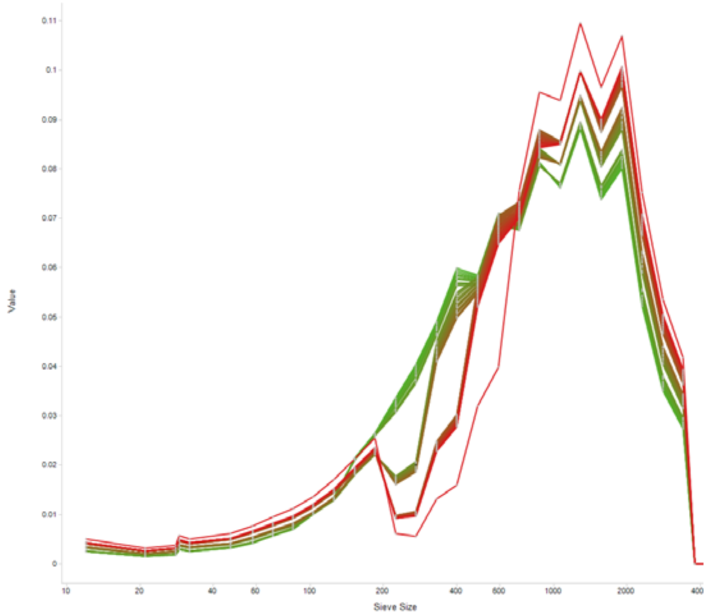


Breakage Rate Constant

Alpha

$$S_M = \begin{cases} Sc_M \left(\frac{y}{y_c}\right)^{\alpha} & \text{for } y \geq y_c \\ 0 & \text{for } y < y_c \end{cases}$$

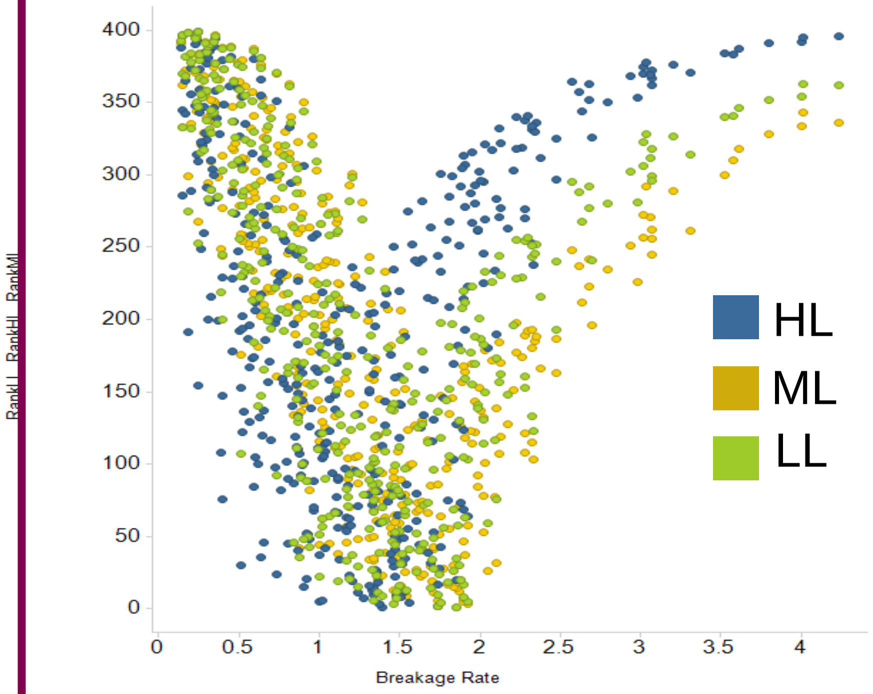
Critical Particle Size



- **Critical particle size**
  - Unusual distribution above 500μm
  - Below this considered physically unrealistic

Breakage rate and Growth rate – GSA ranked proximity to experimental data

Overall Breakage Rate



$$S_M = \begin{cases} Sc_M \left(\frac{y}{y_c}\right)^{\alpha} & \text{for } y \geq y_c \\ 0 & \text{for } y < y_c \end{cases}$$

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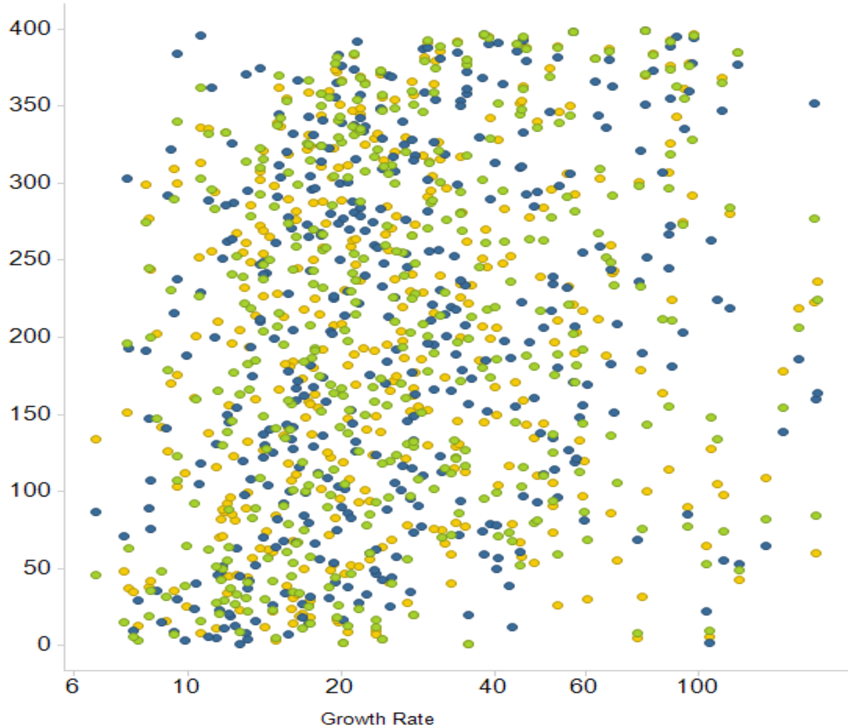
Overall Growth Rate



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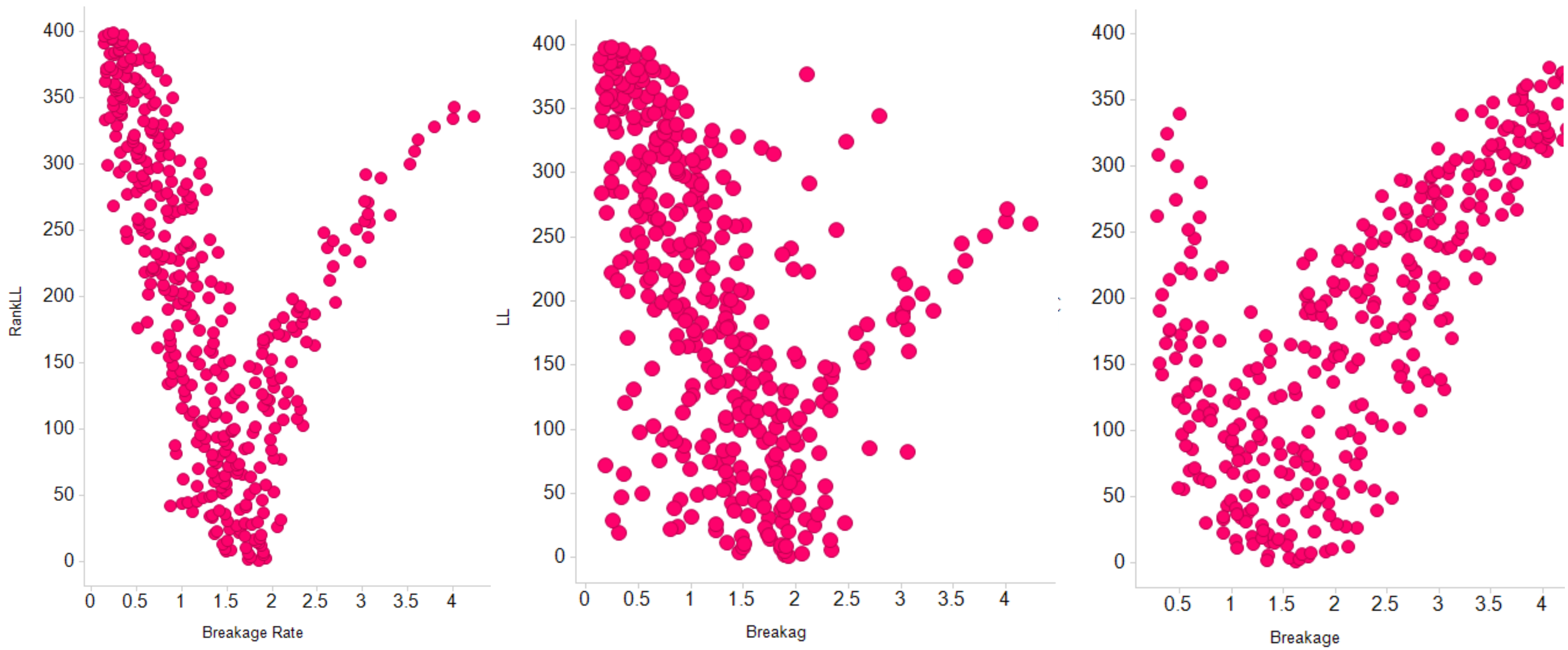
Breakage rate and experimental d50



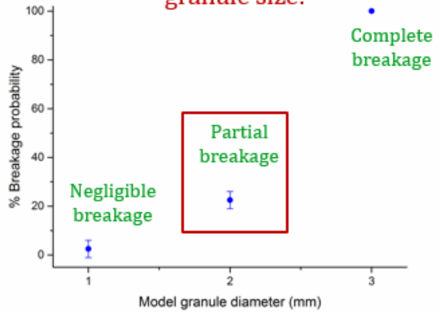
Increasing Experimental D50

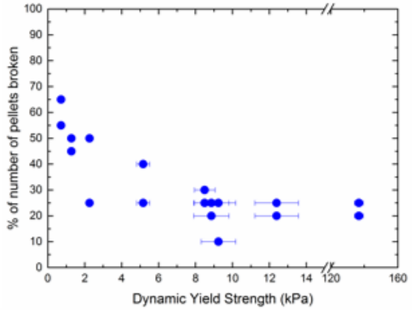
Decreasing Model Optimal Breakage Rate

Significance of breakage in TSG

Breakage in Distributive Mixing Elements

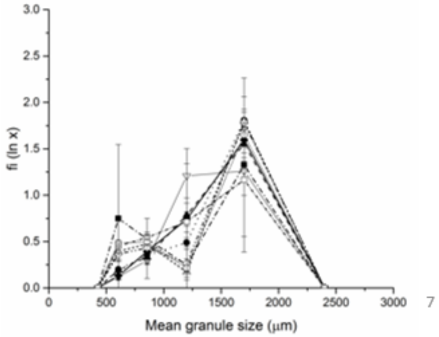
Granule breakage as a function of granule size:



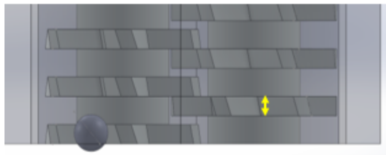


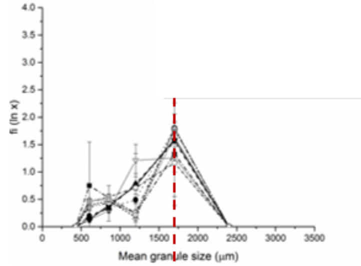
Breakage probability of material stronger than 9 kPa is independent of the dynamic yield strength

Daughter size distribution is independent of material strength

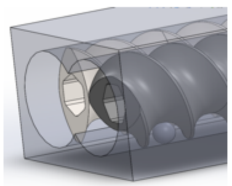


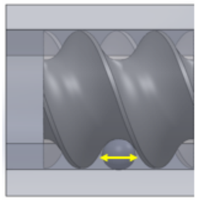
Tailored Granule Design

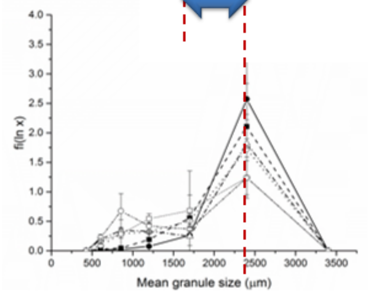




Different particle size using different screw design







'Investigating the effect of Raw Material Properties on the Breakage Rate Process in a Twin Screw Granulator',
S. Pradhan, M. Sen, C. Wassgren, J. Litster, I. Gabbott, G. Reynolds, AIChE Annual Meeting 2016

Summary

- Understanding/Observations
  - Model complexity can be reduced by identifying parameters that don't have a significant effect on output properties
  - Some parameters can't be estimated by only using granule size data (e.g. consolidation rate)
  - Breakage appears to be a dominating mechanism in TSG for granule size

- Some areas for model development
  - Estimated rate parameters are a function of liquid amount
    - Ideally liquid amount would be mechanistically captured by the rate expressions
  - Screw speed is not explicitly captured – this could influence RTD in addition to collision frequency / shear stress

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