Integration of Particle Modelling in Powder Processes

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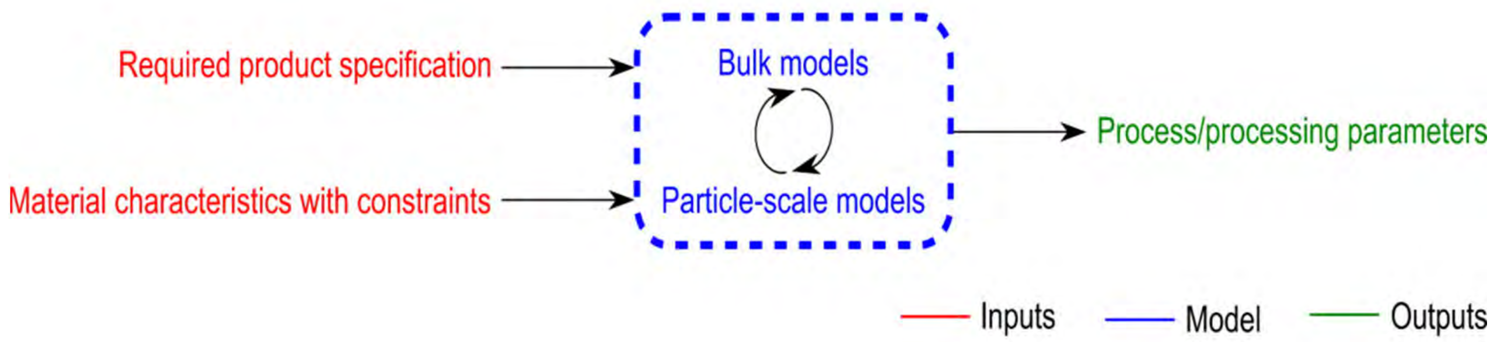
Introduction

The Challenge

- Modelling and simulation increasingly being used as a means to inform and accelerate the development of robust particulate products and processes
- Great advances have been made on many modelling methods across different length scales
- However few academic ‘particle based processing’ models translated into industrial practice



- Need to accelerate industrial adoption to support digital transformation and industrial innovation

MMPP Participant Involvement

Industry Partners

Johnson Matthey

Pfizer

P&G

AstraZeneca

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

Project Management – Pathway to Exploitation

cpi

Advanced Modelling Partners

EDEM

PSE

Know-how:
Experience in commercialising models - modelling platform – model libraries – interfaces for model coupling

Know-how:
provisional models – work-flow development, model validation – prototype model development

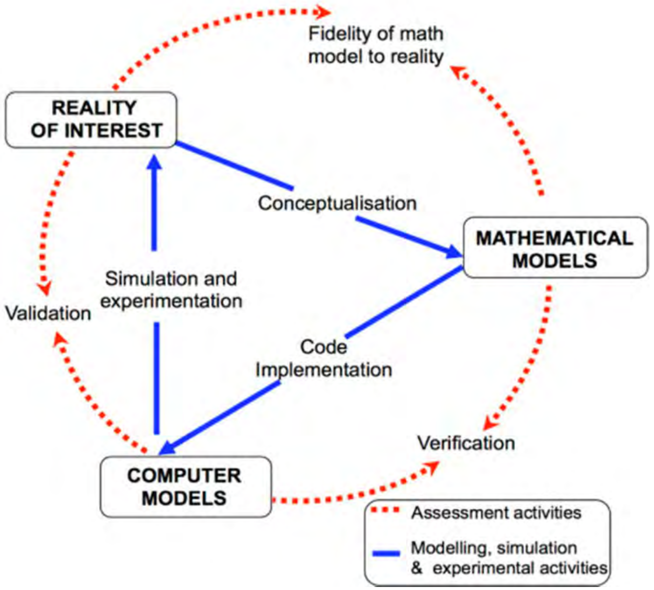
Knowledge Partners

THE UNIVERSITY of EDINBURGH

The University Of Sheffield.

Project goal and objectives

Develop a generic framework for translating particle models of industrial relevance into industrial practice

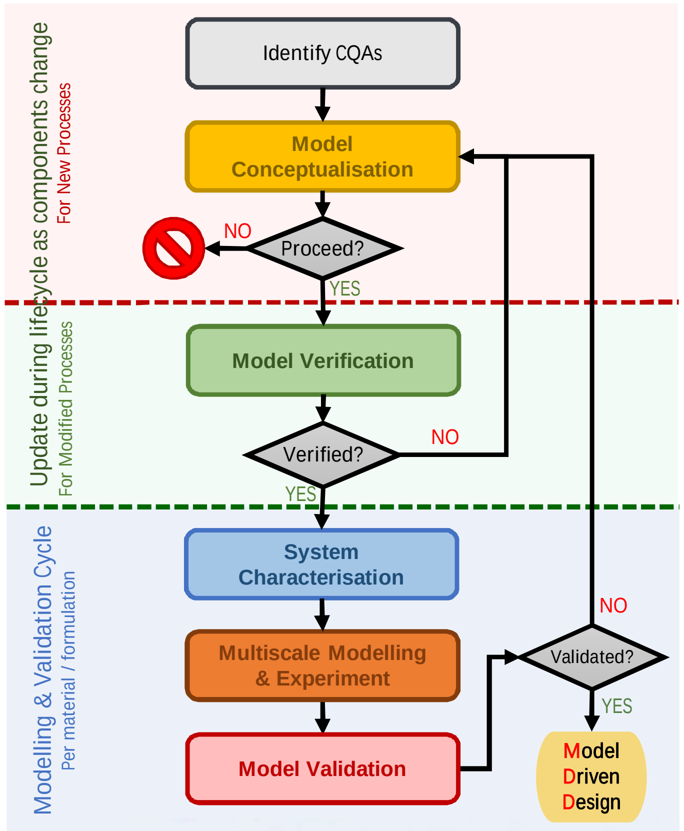


Process of model verification and validation to achieve predictive modelling

- **Decision support tool** for commercial exploitation accessible by companies
- Using wet granulation as exemplar case study
  - prototype and production ready granulation models
- Significant input from industrial partners and software houses to inform the work flow

Generic Framework for Model Driven Design

Generic Framework for Model Driven Design (MDD)



- MDD aligns with achieving Quality by Design (QbD) through sound science
  - What are your product's ***Critical Quality Attributes*** (**CQAs**)?
  - What is the optimal particle model for your process?
  - Is it feasible and resourced to proceed?
  - Have you implemented the model **correctly**?
  - Have the **CMAs** & **CPPs** been captured?
  - Determine the **CQAs** from simulations & experiments
  - Have you implemented the **correct** model?

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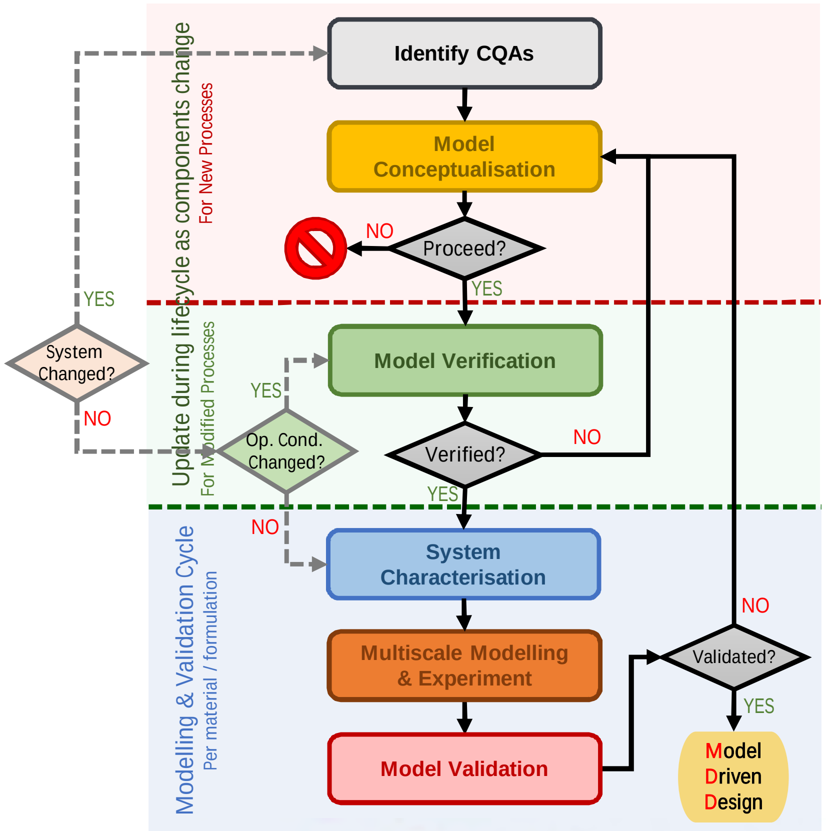
Generic Framework for Model Driven Design



- **Multiple entry points into framework**
  - New System: always start with first stage
  - If the system changes:
    - Significant change
    - Minor change in operating conditions
  - Same system, different material/product

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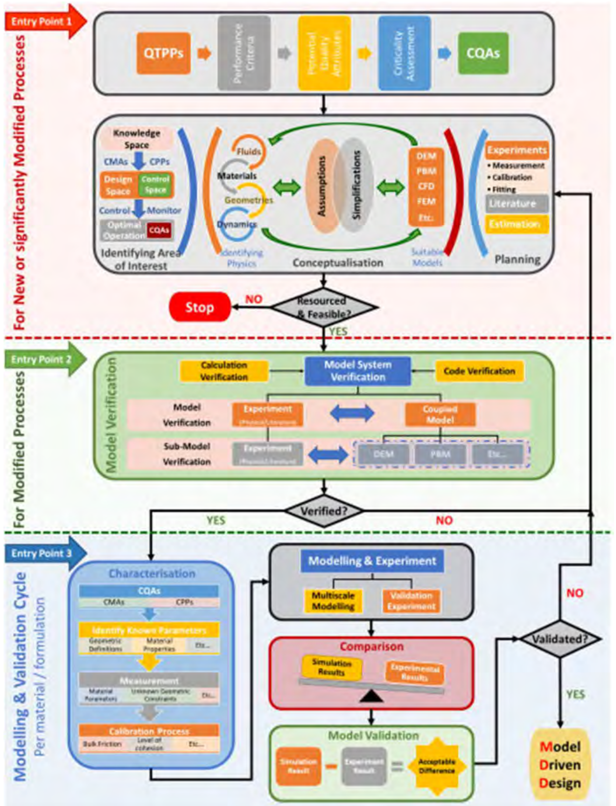
Generic Framework for Model Driven Design



- The generic framework can be considered as two distinct stages:
  - An initial **model definition and verification stage** that only needs to take place when MDD is applied to an operation for the first time or be updated as system components change
  - The **modelling and validation stage** which would be carried out on a per-product basis.

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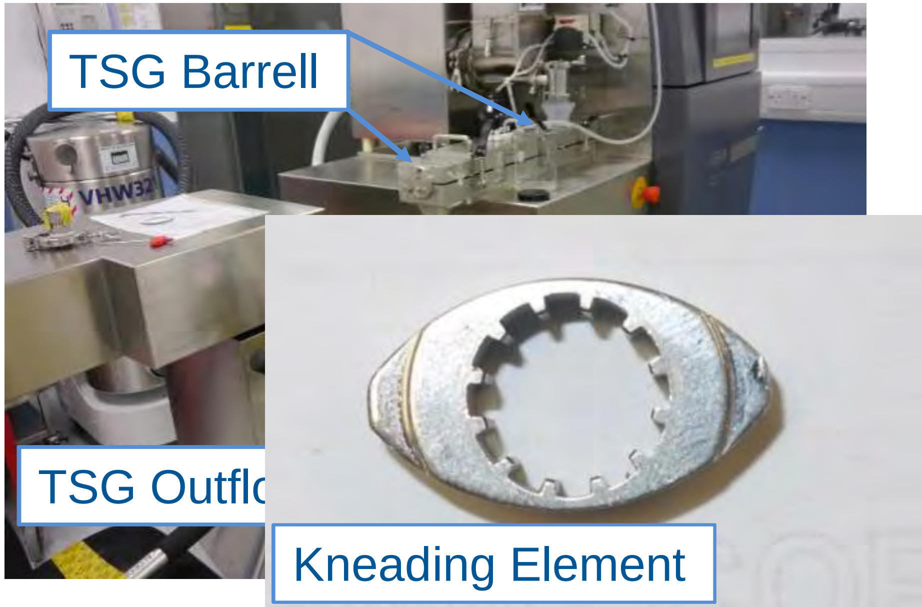
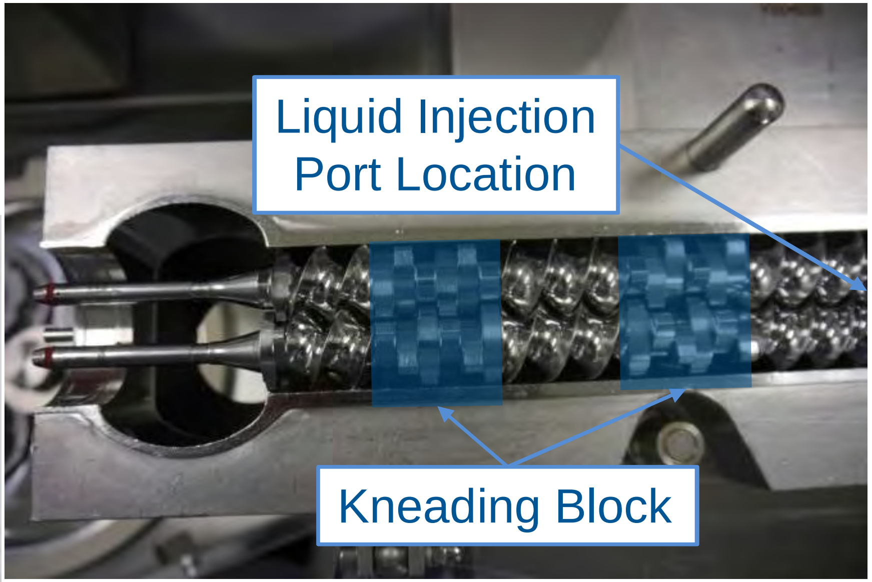
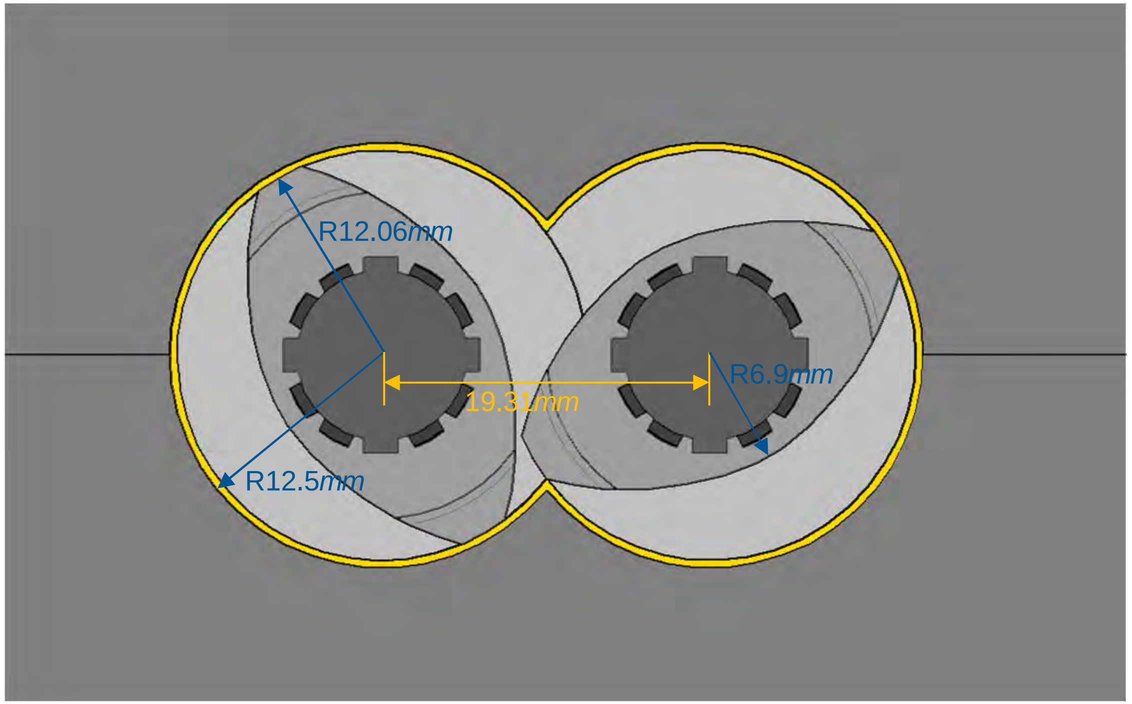
GEA ConsiGma 1 Twin Screw Granulator (TSG)



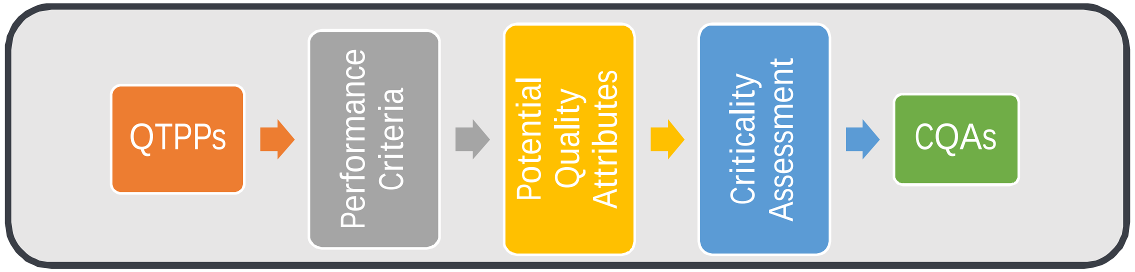


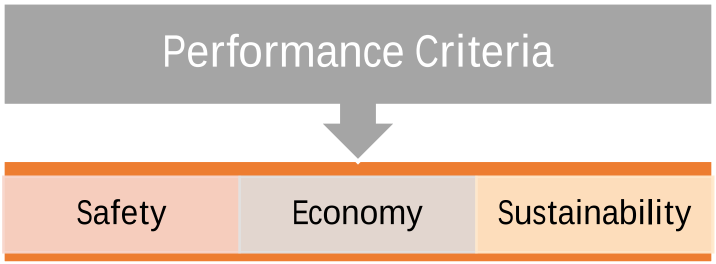
GEA ConsiGma 1 TSG



- Screw Diameter: 25mm
- Barrel-Screw Clearance: 0.44mm
- Screw-Screw Clearance: 0.175mm
- Screw Lead: 25mm
- Total Screw Length: 497mm

Identifying the CQA's for ConsiGma Twin Screw Granulator

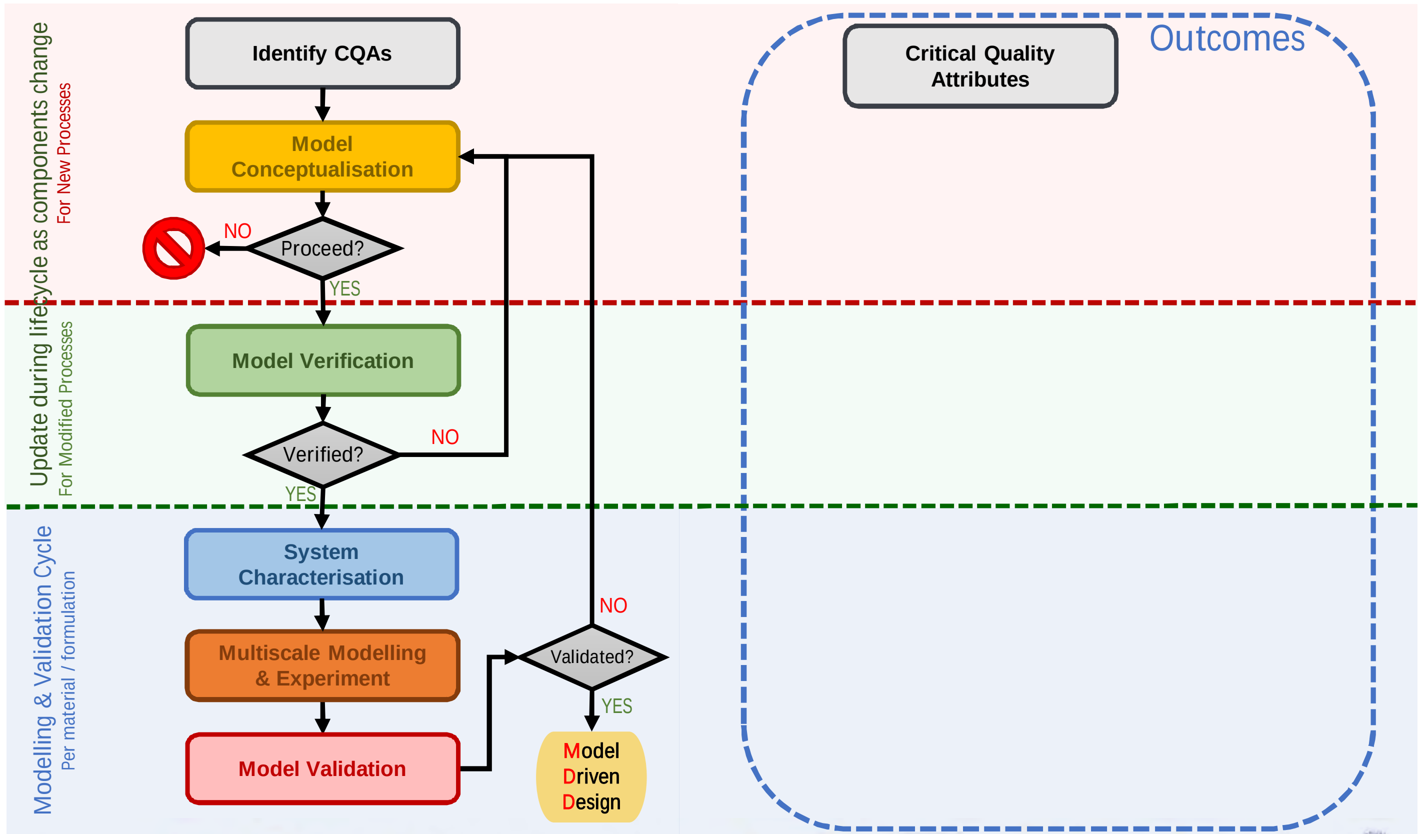




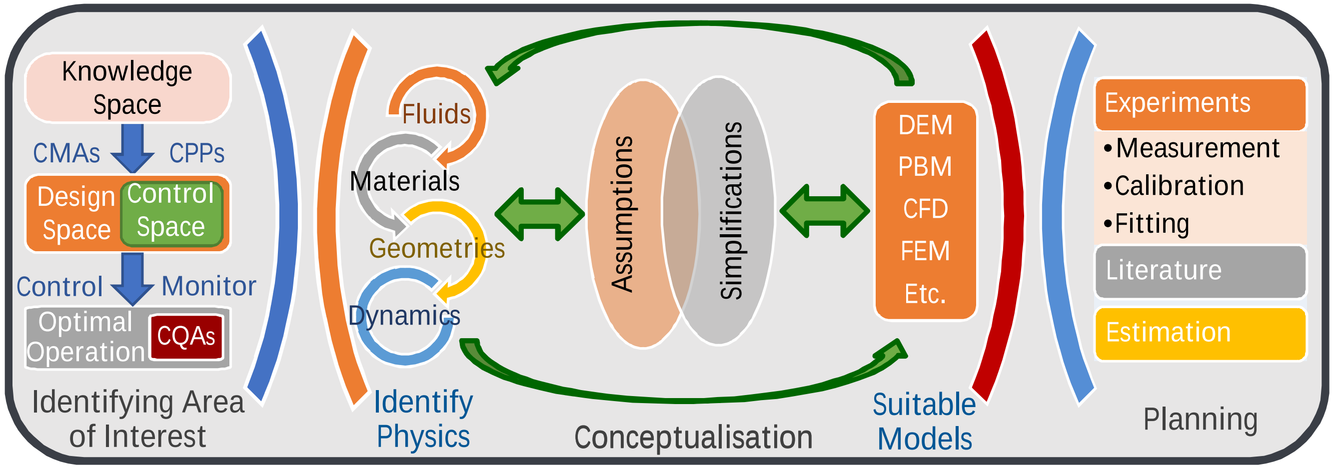
- The **Critical Quality Attributes (CQAs)** are the quality attributes to ensure product quality
  - they *inform* the product and process development
- Influenced by **CMAs** & **CPPs**.

- For **TSG** *granule size distribution* and *granule porosity* are granulation **CQAs**

Generic Framework for Model Driven Design

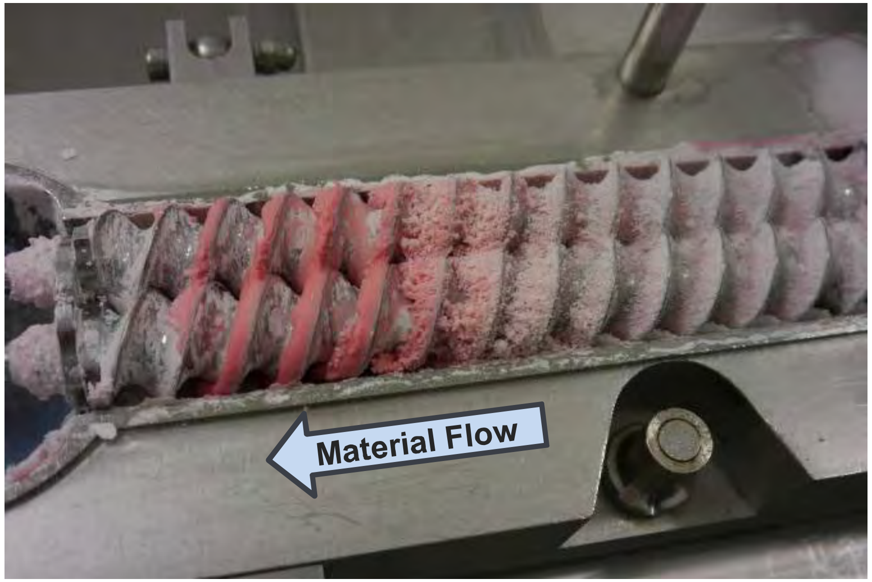


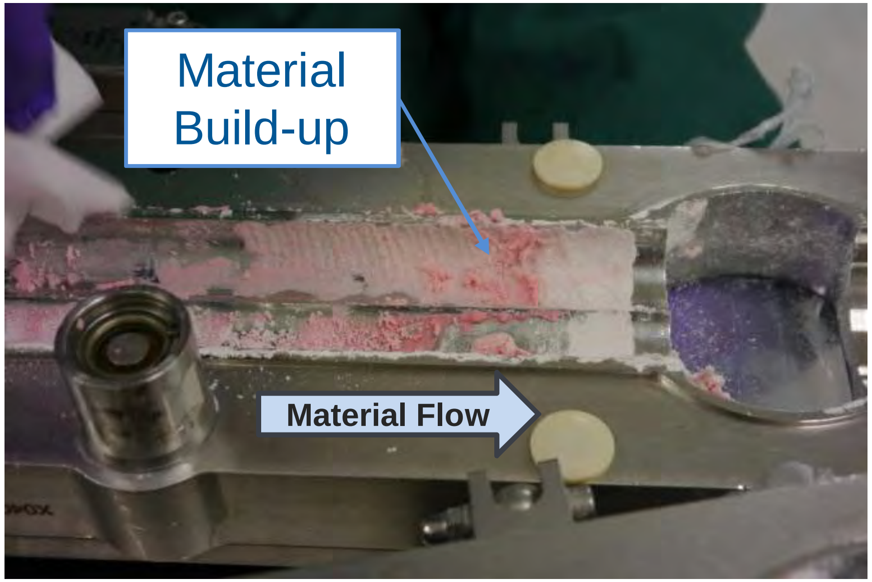
Conceptualising the model



- Requires **knowledge and understanding** of the system
  - Identifying physics that have little effect is just as important as identifying ones with large effects
- **Care** is required at this stage to not make any assumptions or simplifications that may be damaging to the final output
- The process may lead to new physics (models) being implemented or developed if existing models are deemed unsatisfactory or lacking
  - What physics do current models capture?

GEA ConsiGma 1 Twin Screw Granulator





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Model Conceptualisation Process

Identifying The Area of Interest

- Identify the **process** to be modelled, the **purpose** and desired **outputs**
  - What are the *constraints* / degrees of freedom of the problem?
  - Allows simplification through specificity

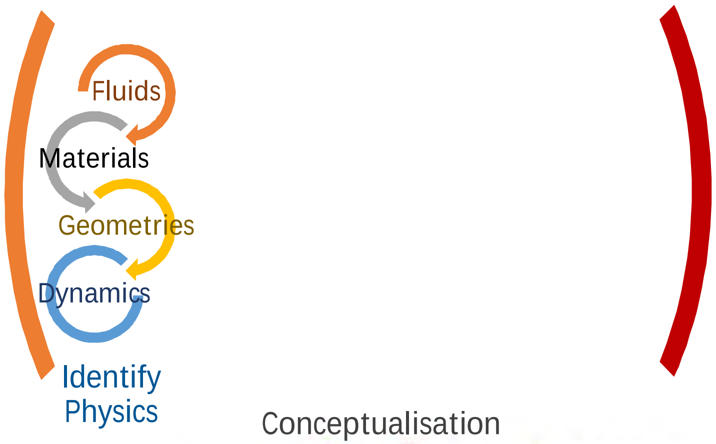
Identifying The Area of Interest

- **Process**
  - Wet Granulation (TSG)
- **Purpose**
  - Guide for scale up and formulation design
  - Improve experimental design
  - Enhance process understanding
- **Outputs**
  - Granule size distribution and other attributes as a function of process parameters and formulation properties
- **Constraints**
  - Narrow operating window of L/S ratios
  - Limited variation in Feed-rate
  - Geometry Interaction

Model Conceptualisation Process

Identify the Physics of the Problem

- What are the **key physics**?
- How can physics be captured in models?
  - Particle based methods
  - Fluid Interactions….etc….



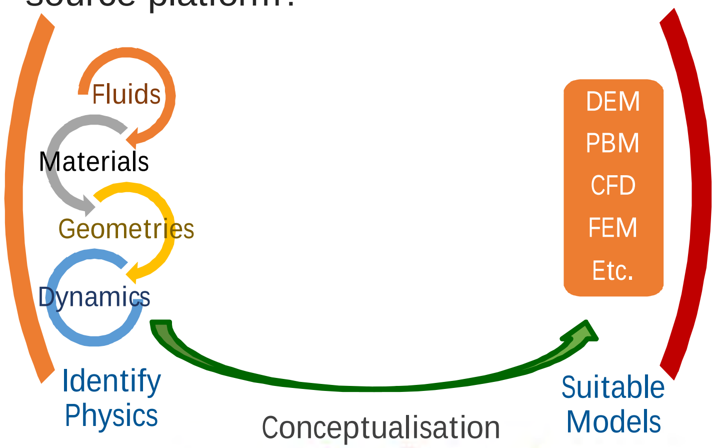
Key Physics

- Liquid Addition - affects cohesion
- Geometric Definition - Particles passing through tight gaps?
- Screw dynamics (RPM) – RTD, Agglomeration rate
- Fill level / feed rate – Affect particle dynamics
- Screw configuration
  - Different screw elements behave very differently (compartmental approach needed)
  - Affects RTD, Rate Processes, Agglomerate size
- Nucleation and breakage are key processes
- Kernel selection for compartments:
  - Any number of nucleation, layering, breakage consolidation kernels
  - Dependent on screw configuration

Model Conceptualisation Process

Identify Suitable Models

- Are they **fit for purpose**?
- Does the model **need modification**?
- Are they available in a commercial or open-source platform?



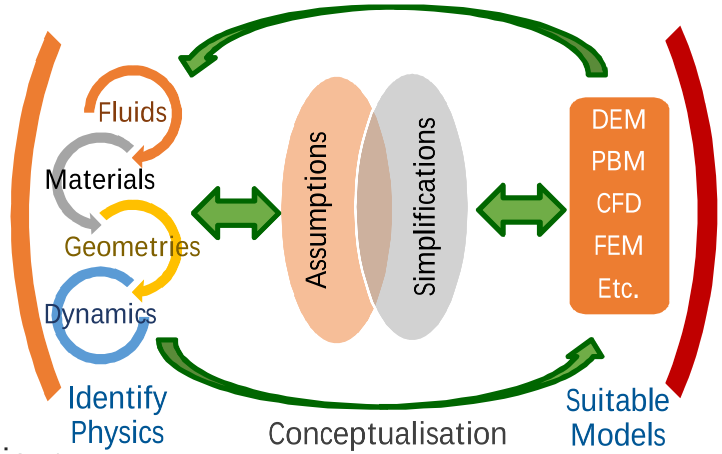
Exploring Existing Models

- **FEM, CFD, DEM, LBM, SPH, PBM, …..??**

Suggested Approach

- **Particle Scale Model (DEM):**
  - Can capture particle level physics and complex machine dynamics
  - DEM simulations can provide RT as a function of process parameters for input to PBM model
  - Cohesion can be included
- **Process Level Model (PBM):**
  - gFormulate TSG model incorporates correct rate processes and allows compartmental approach
  - Breakage kernel not fit for purpose
  - Mean residence time is an input parameter
  - PBM provides temporal scale-up

Model Conceptualisation Process

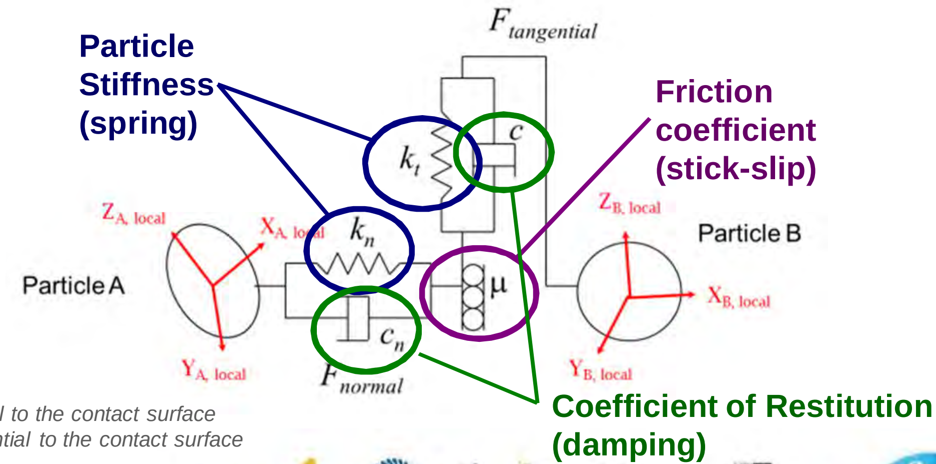


Assumptions & Simplifications

- Particle shape not important – simplify using sphere
- Not fully wet system
  - No need for CFD coupling
  - Cohesive contact model to capture agglomeration behaviour
- Computation Efficiency
  - Conveying zones of limited interest and importance (reduced size DEM model)
  - Periodic?
- Similar elements can be grouped together in PBM compartments?
- Temporal scale-up provided by PBM
  - DEM provides key input parameters

DEM - capturing particle level physics

- Discrete Element Method (DEM) models the motion and interaction of all individual particles in a system
  - Solves equations of motion with appropriate particle contact model
  - Can account for breakage, cohesion, liquid effects, etc
- Explicit time-stepping algorithm *(Cundall & Strack, 1979)*

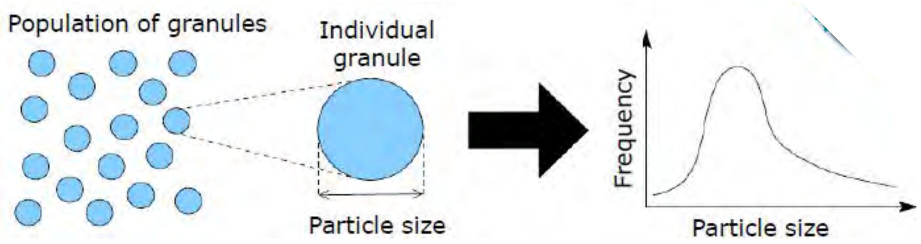


n = normal to the contact surface
t = tangential to the contact surface

- **Developments**:
  - From 2D discs to 3D spherical particles
  - From spheres to non-spherical:
    - Ellipsoids
    - Multi-spheres
    - Polyhedra
    - Super-quadrics
  - From elastic to elasto-plastic, cohesionless to cohesive, bonded, sintered, wetted, etc…
    - To capture complex particle phenomena
  - From simple particle problems to complex multiscale, multiphysics problems (CFD, FEM, MBD, etc)

PBM – Scaling up to industrial time and length-scales

- **Population Balance Model** (***PBM***) can track particle attributes in each size class based on sub-process rate expressions
  - Typically empirical or semi-empirical
  - Failure to account for process and material properties
- Spatial information is not inherent:
  - Compartmental approached needed
  - Inhomogeneous liquid distribution
- **Many** parameters need to be ***estimated*** from the experimental data



After Barrasso (2015)

PBM model for granulation

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

$$\frac{\partial}{\partial t}n(s,l,g,t) + \frac{\partial}{\partial s}\left[n(s,l,g,t)\frac{ds}{dt}\right] + \frac{\partial}{\partial l}\left[n(s,l,g,t)\frac{dl}{dt}\right] + \frac{\partial}{\partial g}\left[n(s,l,g,t)\frac{dg}{dt}\right]$$

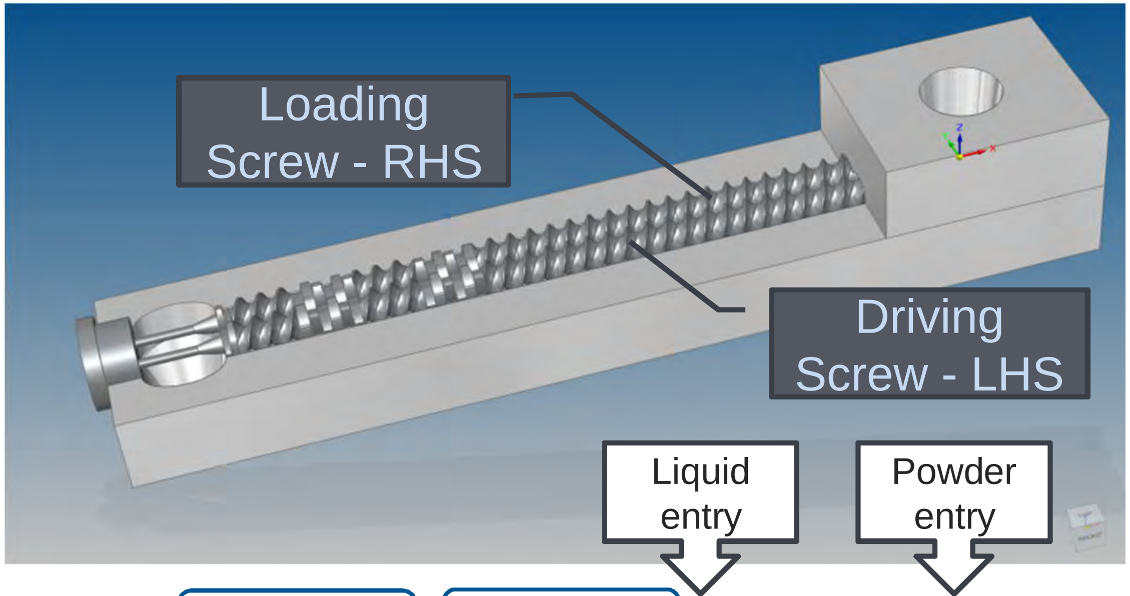
$$= B_{nuc}(s,l,g,t) + B_{break}(s,l,g,t) - D_{break}(s,l,g,t) + \dot{F_{in}} - \dot{F_{out}}$$

- $n(s,l,g,t)$: 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

Coupled Contributions

- **PBM Simulations:**
  - Groups particles into different classes based on their properties and tracks the size and number of particles over time
  - Computationally inexpensive
- **DEM Simulations:**
  - Provide particle scale data such as collisions data, impact energy or residence time to inform the PBM
  - Considers the effect of the equipment geometry and its dynamics on the system

GEA ConsiGma 1 TSG Model Representation



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	25	26	27	28
Type	K 1/6"	K 1/6"	T 1.5	K 1/4"	K 1/4"	K 1/4"	K 1/4"	K 1/4"	K 1/4"	T 1.5"	K 1/4"	K 1/4"	K 1/4"	K 1/4"	K 1/4"	K 1/4"	T 1.0"	T 1.0"	T 1.5"	T 1.5"	T 2.0"	T 2.0"	T 2.0"	T 2.0"	K 1/6"	Bush	coupler	Bolt
angle	0	+60	0	0	+60	+60	+60	+60	+60	0	0	+60	+60	+60	+60	+60	0	0	0	0	0	0	0	0	0	0	0	0

Kneading Block 2

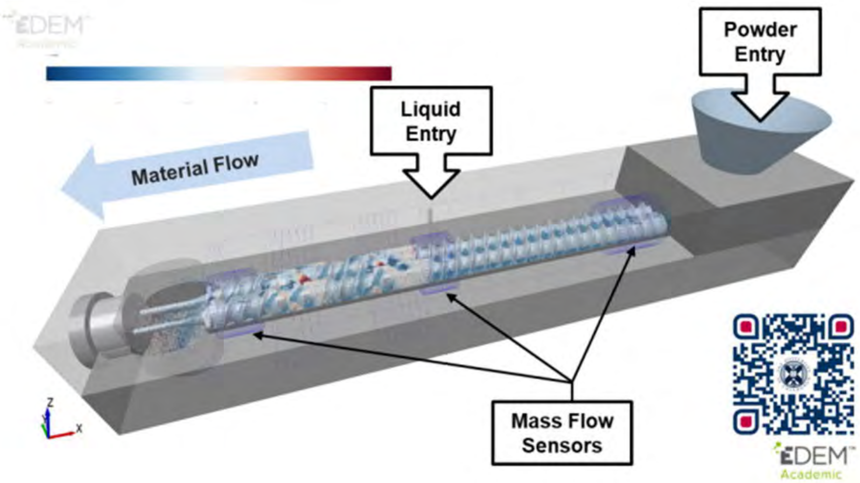
Kneading Block 1

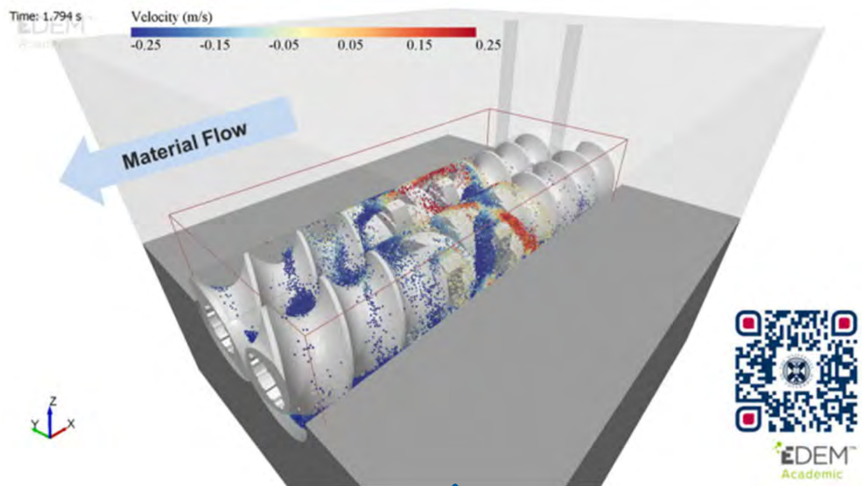
Material flow

K 1/6 " is denoted as one sixth inch kneader element
K 1/4 " is denoted as one quarter inch kneader element
T 1.0 " is denoted as one inch conveying element
T 1.5 " is denoted as one and a half inches conveying element
T 2.0 " is denoted as two inches conveying element

Kneading zone angle at +60 degree

Conceptualisation of TSG in DEM Model





Reduced to smaller compartments where possible

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”

C1: N

C2: B+L+C

C3: B+L

C4: B+L+C

C5: B+L

C6: B+L+C

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:

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

$\dot{F_{out}}$ is the outlet flow rate of the unit;
F is mass in the unit;
τ: 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

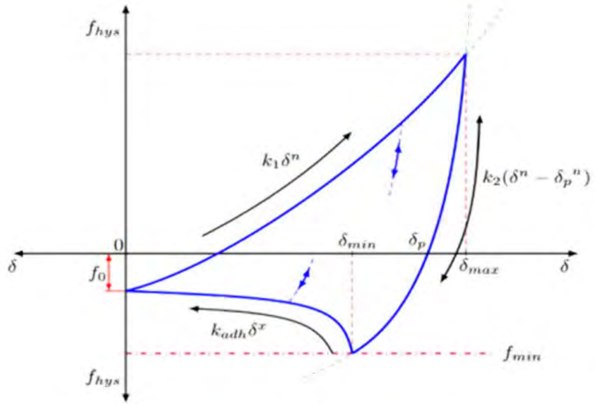
– The residence time τ would be estimated from DEM (Barrasso and Ramachandran, 2016)

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

Multiscale DEM-PBM Model for TSG

DEM results informing PBM model via coupling

Existing Model Evaluation	Most suitable model(s) for TSG	
	PBM	DEM
Identify the appropriate models	Nucleation	Edinburgh Elasto-Plastic Adhesion Model
	Breakage (Modification required)	
	Layering	
	Consolidation	



Rate Processing Kernels

Nucleation — Conveying

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

Barrasso et al., 2015

Layering — Conveying & Kneading

Cameron et al., 2005

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

Breakage — Conveying & Kneading

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

Developed breakage kernel

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

Consolidation — Kneading

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

Iveson et al., 1996

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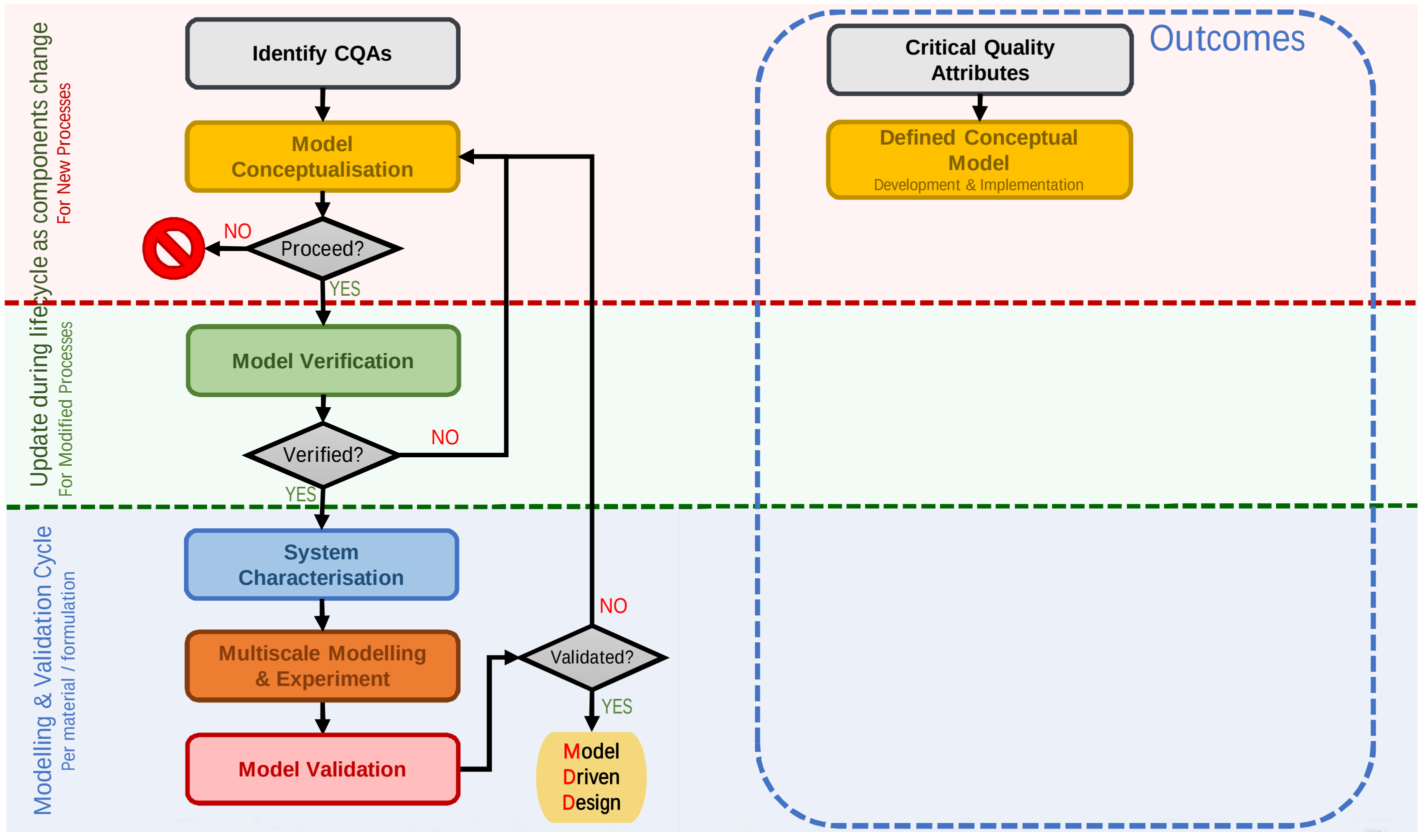
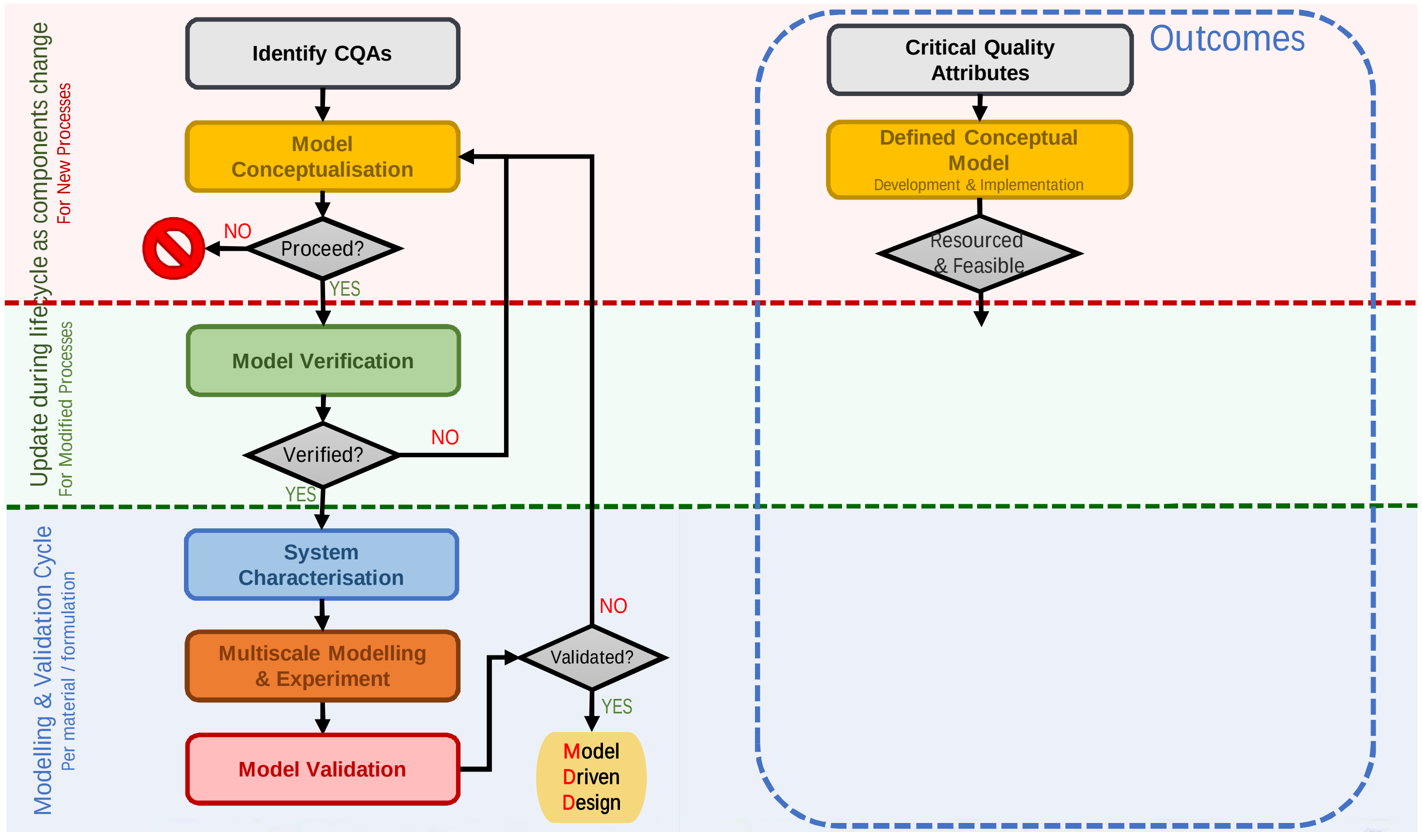


Decision Point

Is it worthwhile proceeding?

- Do I own the software platform or is it worth buying?
- What is the cost (time and money) of making the necessary changes to the model?
- Is sufficient expertise available (in the company, by consultancy, …)?

Generic Framework for Model Driven Design



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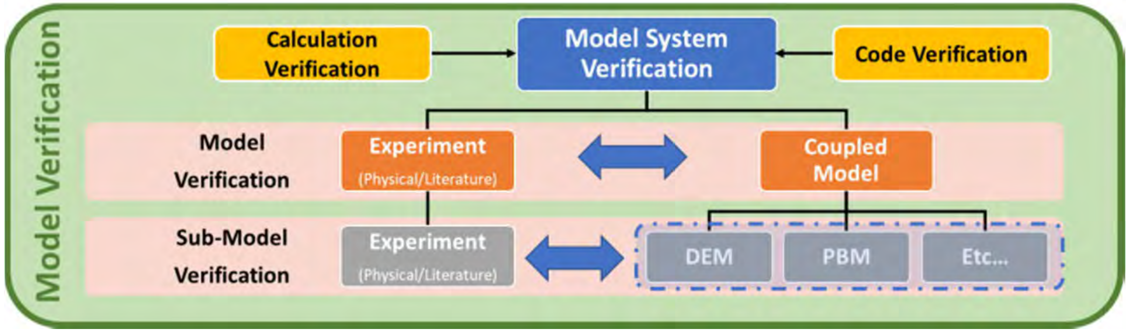
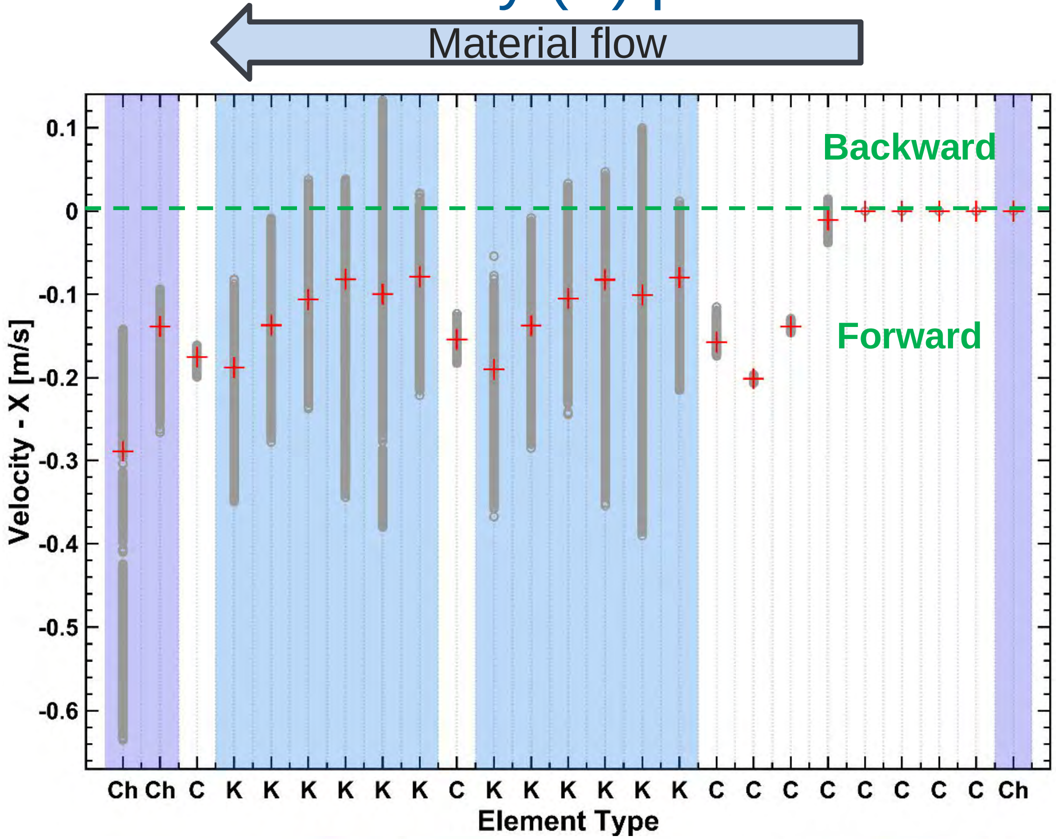
Model Verification



- Considering three levels of verification:
  - Code verification
    - Coding – error free implementation
  - Calculation verification
    - Model fidelity – numerical error
  - **Model system verification**
    - Bottom-up approach starting with the sub-models
    - Identify component of the multiscale model that may not be performing well
    - Provide early check on the appropriateness of the model

DEM Sub-model Results

Translation Velocity (X) per Element



- Negative demotes material moving forward
- Significant reverse flow occurring on second kneading element
  - Some reverse flow 1st, 3rd and 4th elements

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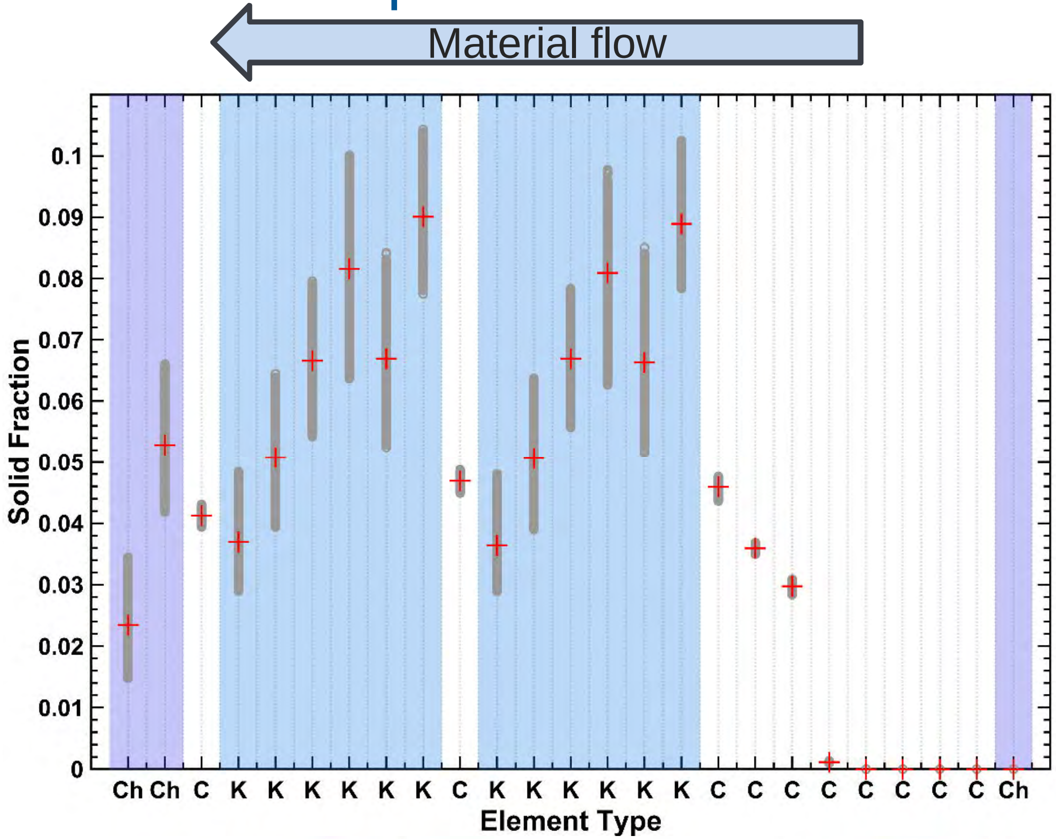
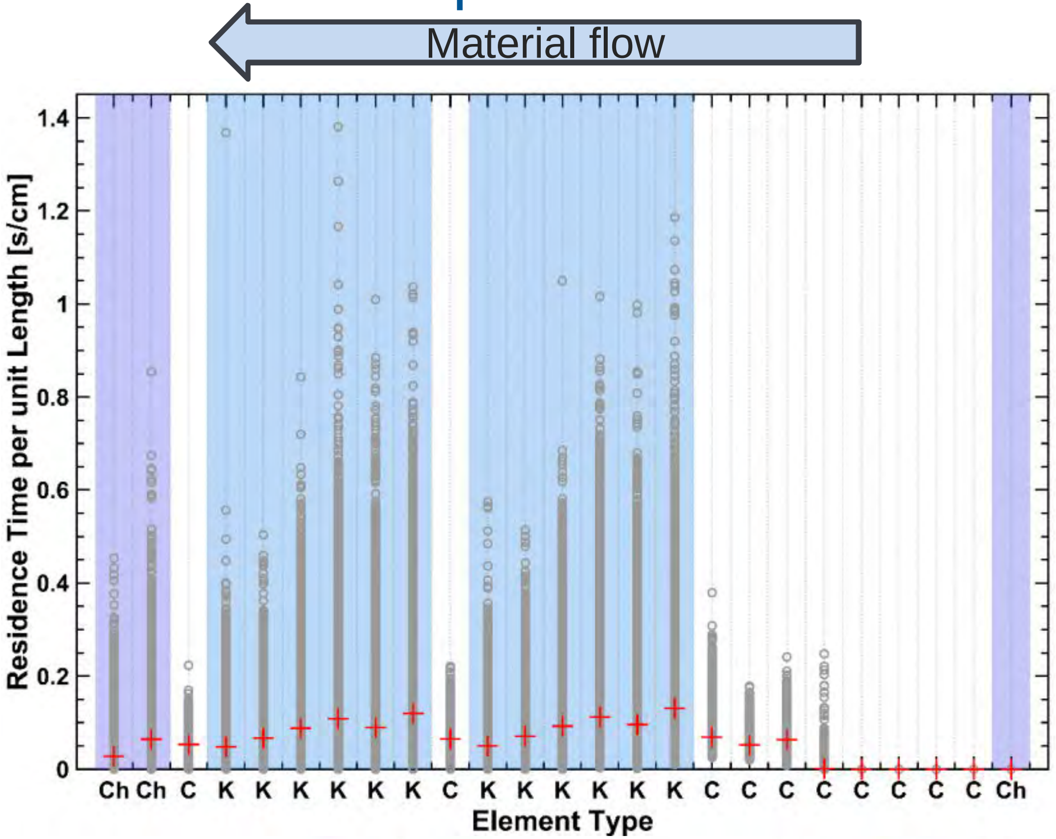
Solid Fraction per Element



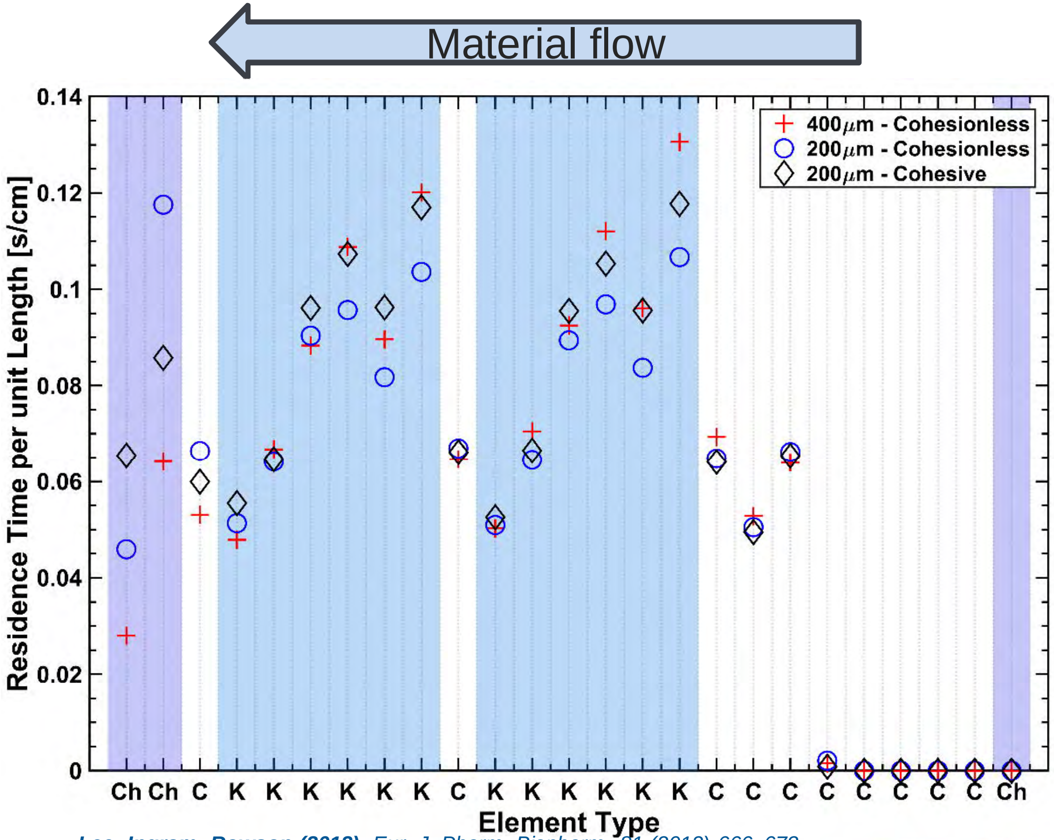
- Highest solid fraction found at kneading elements where material is '*held up*'
- Latter kneading elements have similar solid fraction to conveying element
- Significantly lower solid fraction on 2nd kneading element

Residence Time per Element



- Slightly higher for kneading elements
- Possibly something interesting happening at transition from conveying to kneading elements
  - Residence time on first kneading element significantly higher
  - Gradual reduction
- Much larger variation in time spent at kneading elements

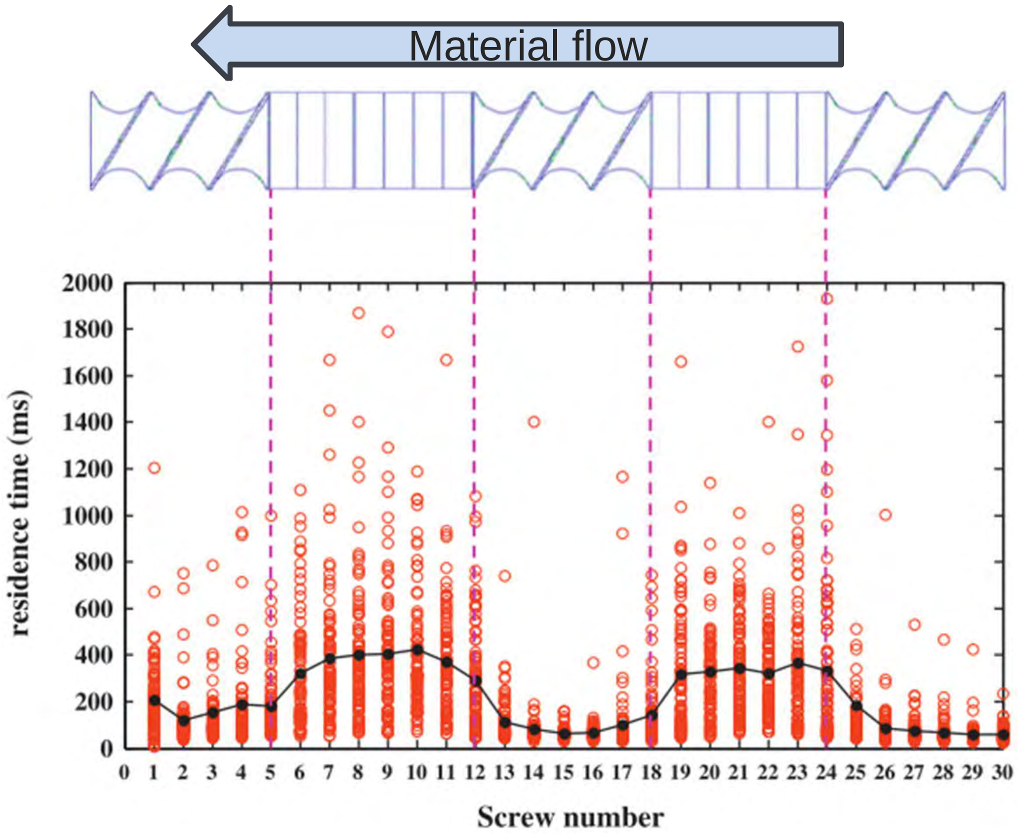
Residence Time Estimation



Lee, Ingram, Rowson (2012), *Eur. J. Pharm. Biopharm. 81 (2012) 666–673*

- Comparable with PEPT experimental data
  - Different screw dimensions and configuration
- Similar trends observed in terms of residence time by element type and observed scatter in measurement

Residence Time Estimation



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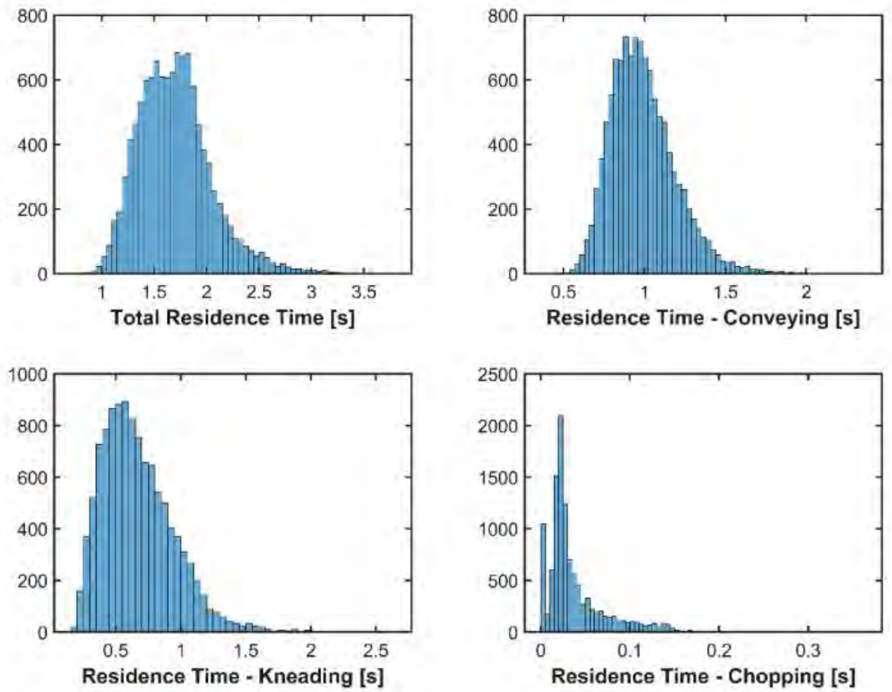
Residence Time Distribution



- Residence Time for ConsiGma 25 at 600 RPM is approximately 1.9s at steady-state
- Mean Residence Time per unit length is higher (≈2x) on **Kneading** elements

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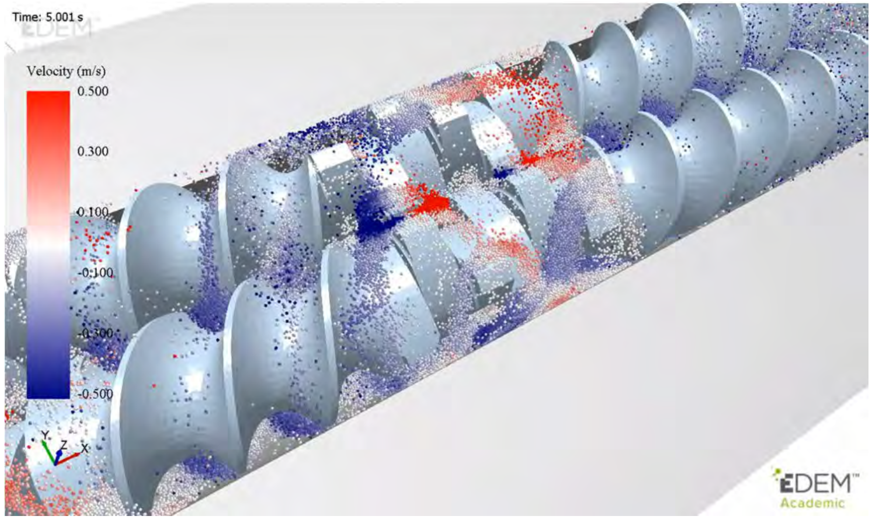
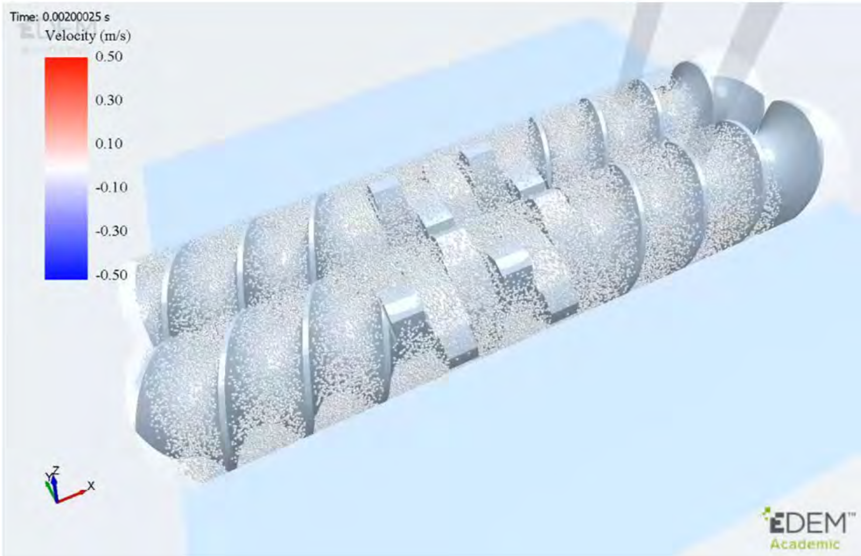
Full & Periodic Simulation Comparison





Full Simulation

Periodic Simulation

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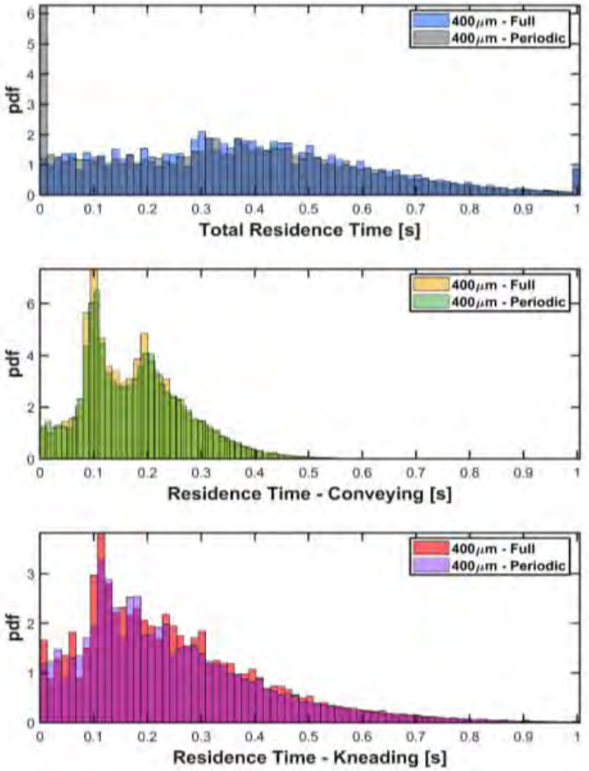
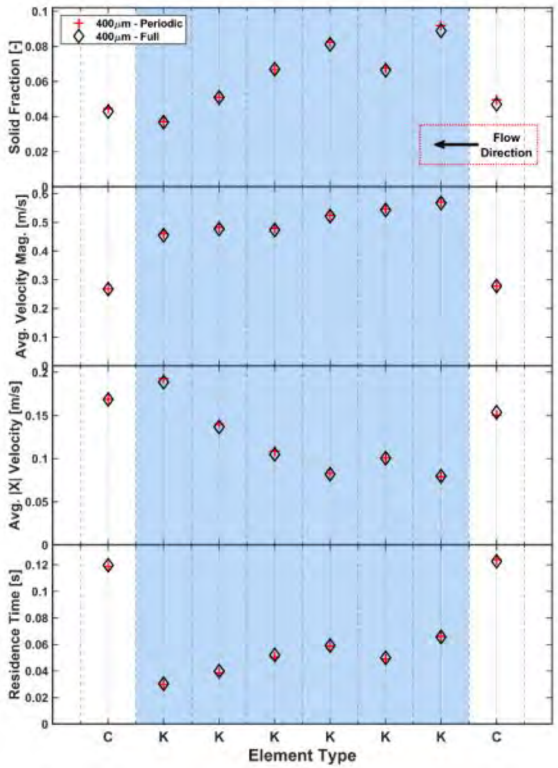
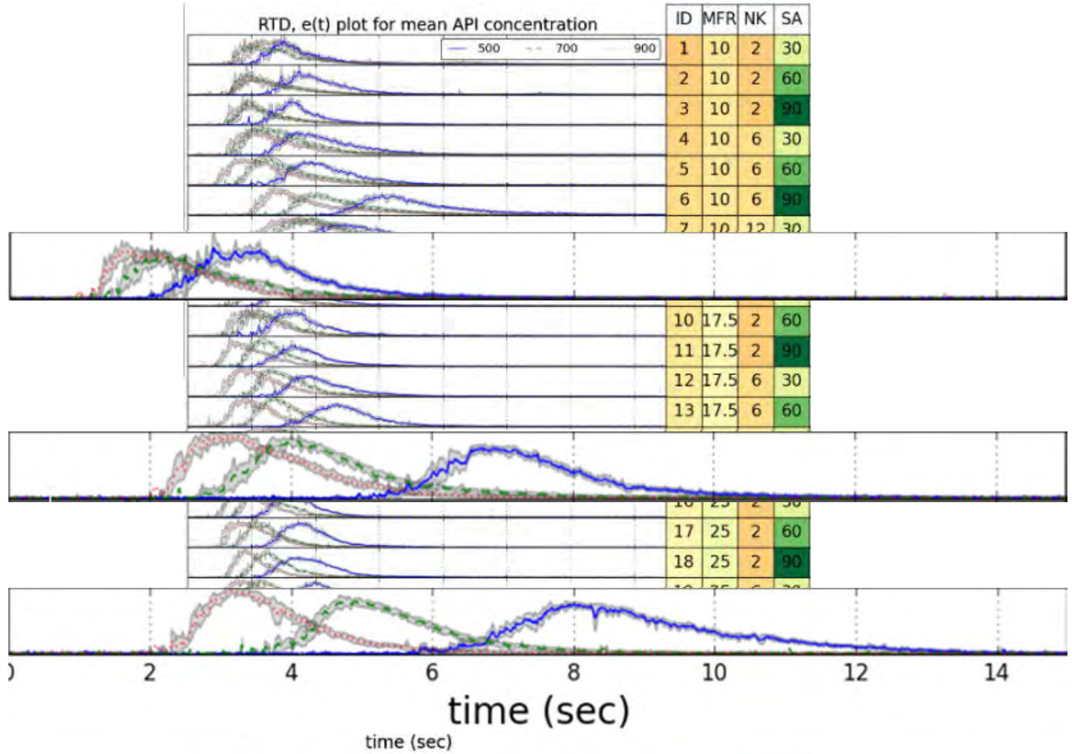
Comparison of Full & Compartmental Models





- Excellent correlation between compartmental model and full scale model
  - Significant time saving

Experimental Studies on ConsiGma 25



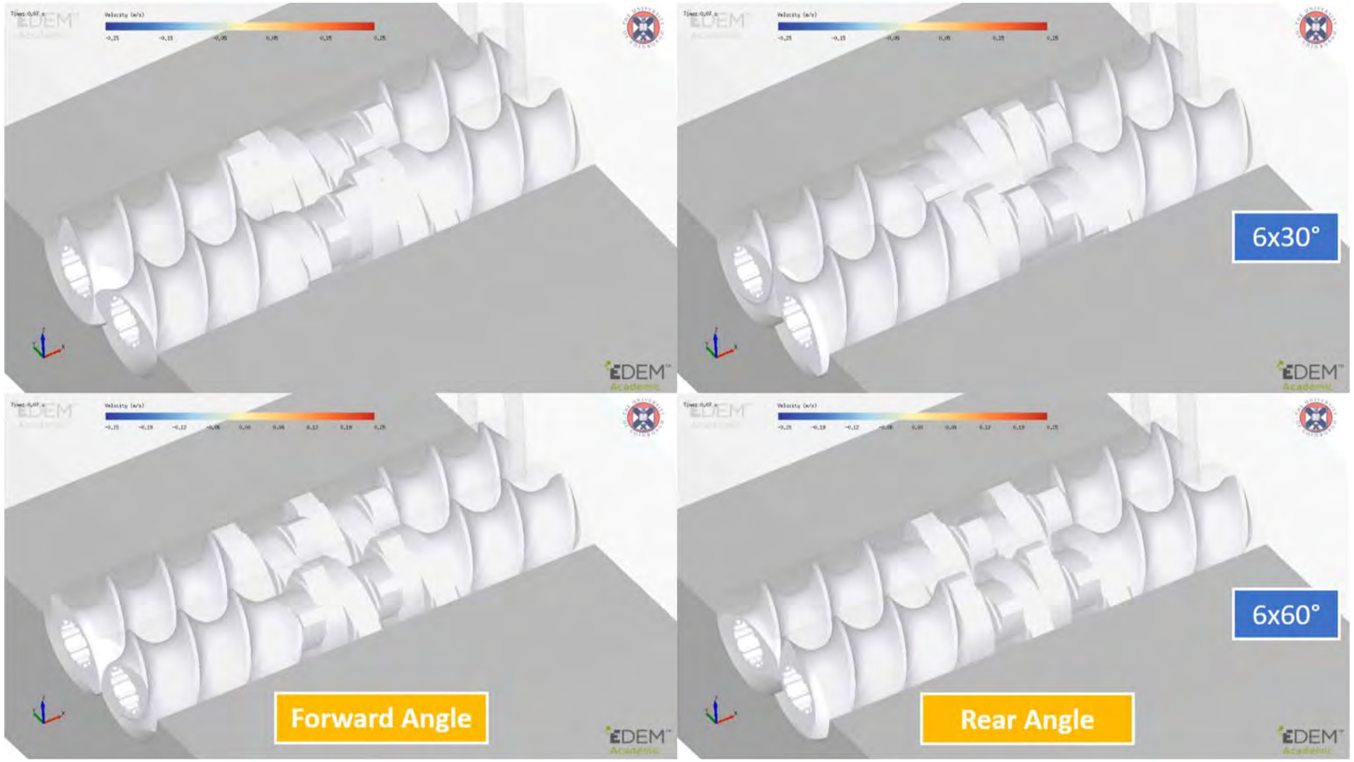
Kumar et al. (2014), European Journal of Pharmaceutics and Biopharmaceutics 87 (2014) 279–289

- Study at various feed rates on Pharmatose® 200M (mean diameter ≈ 50µm) and kneading configurations on ConsiGma 25

MFR	RPM	
	500	700	900
10	5.5	3.5	3
17.5	6.75	4	3
25	8	4.75	3.25

- Interpolating for 14.4 kg/h and 600 RPM gives approximately 5.01s for ***full*** screw length (**N.B.** injection point to measurement point – longer than DEM model)

Exploitation of New Knowledge: Screw Configuration Comparison



Concluding remarks

- This project has successfully created a framework for conceptualising, characterisation and modelling of large scale industrial processes
- In this exemplar case study, DEM provides the particle science to inform the *physics* of the problem
- PBM provides the upscaling methodology to industrial scale
- The proposed Framework provides a platform for
  - developing best practice in model driven design/optimisation
  - progressively replacing empiricisms in our particle based models

Thank you...

PTF7: 7th UK-China-International Particle Technology Forum

- **7th *UK–China International Particle Technology Forum*** and annual ***UK Particle Technology Forum*** will be held jointly in Edinburgh on ***28–31 July 2019***
  - **Information available at www.ptf7.eng.ed.ac.uk**

- This UK-China forum began in 2007 (*Leeds/UK*), and has alternated between China and the UK since then:
  - Guiyang (2009), Birmingham (2011), Shanghai (2013), Leeds (2015) and Yangzhou (2017)
  - International included in title since 2013

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PTF7: Call for Papers

Conference themes to include:

- Particle design, characterisation and measurement
- Particulate processes and manufacturing
- Multiscale and multiphase modelling and simulation
- Geotechnical and environmental applications and processes
- Particle technology in energy engineering applications
- Emerging technologies and novel engineering applications

- **IChemE Young Researcher Award**
- **Best Poster Award**

A **2 page Extended Abstract** should be submitted before **January 31st, 2019**.

Extended abstracts should be submitted for either a poster or an oral presentation.

March 1st, 2019 - Notification of abstract acceptance

May 1st, 2019 - End of ***early bird discounted*** registration

Gran EDI

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DEM-PBM Multiscale Model

One-way Coupling

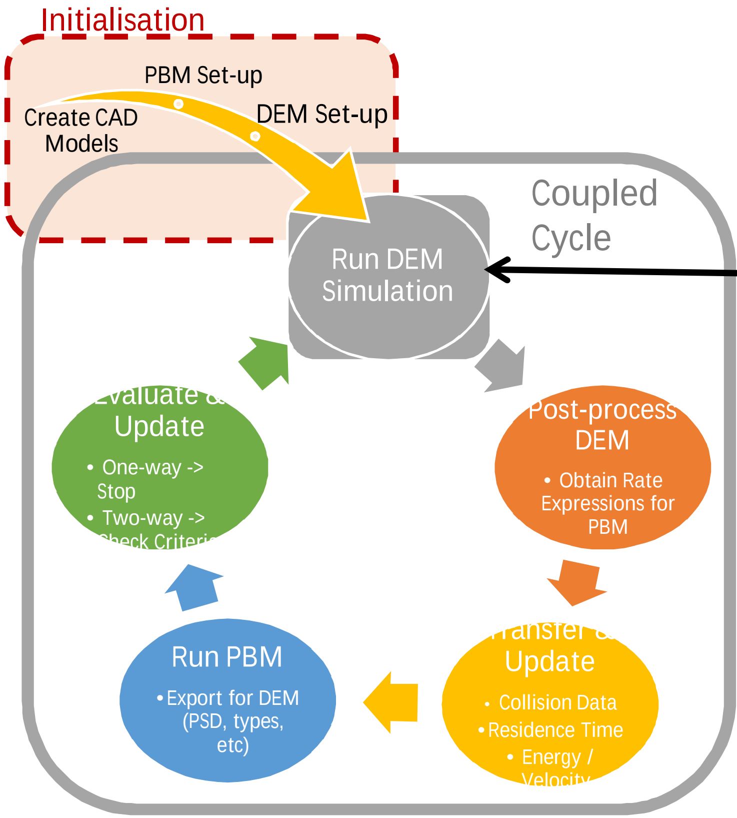
- Suitable in certain applications (Rate processes dominated by geometry setup / Particle size independent)
- When domain can't be simplified to smaller representative compartmental models
- Computationally Inexpensive

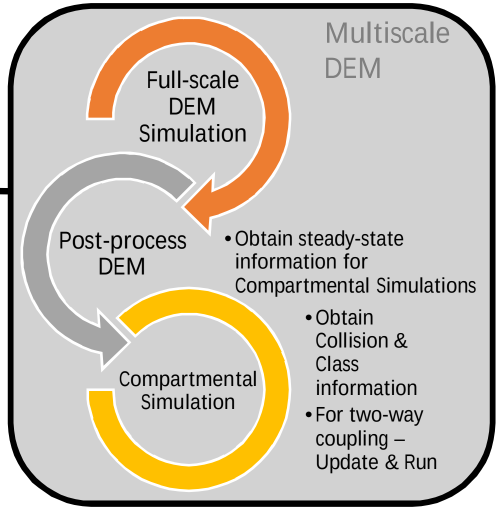
Two-way Coupling

- Large computational cost due to repeated cycles
- Representative compartmental models utilized when possible
- Dynamic or long duration systems

Two-way Coupling (Offline)

- Look-up database of previous results
- PBM interpolates parameters from database instead of calling DEM simulations
- DEM Simulations can be run ahead of time in isolation
- Results can be stored in normal one/two-way coupling to build database





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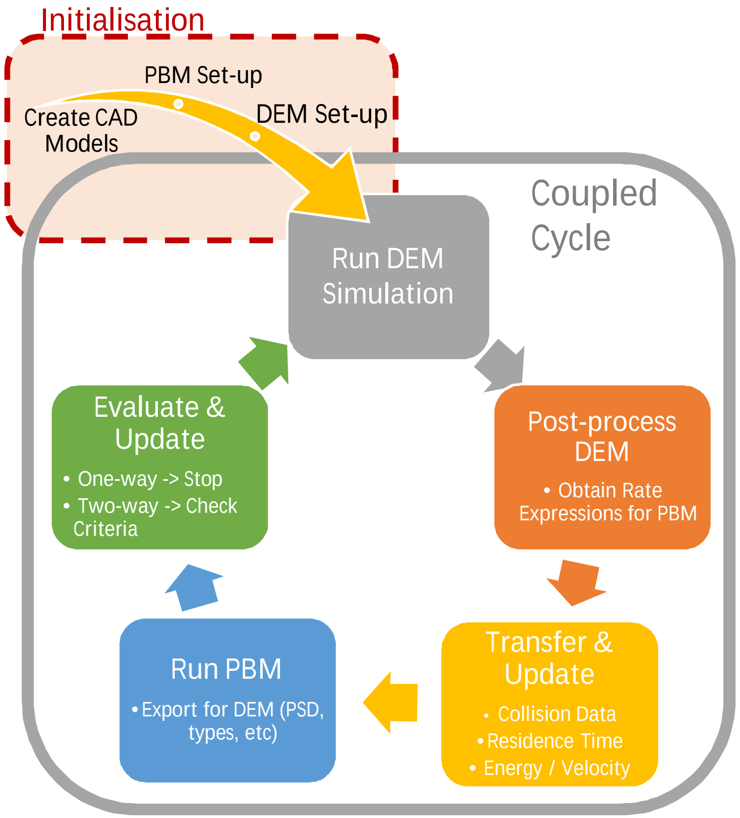

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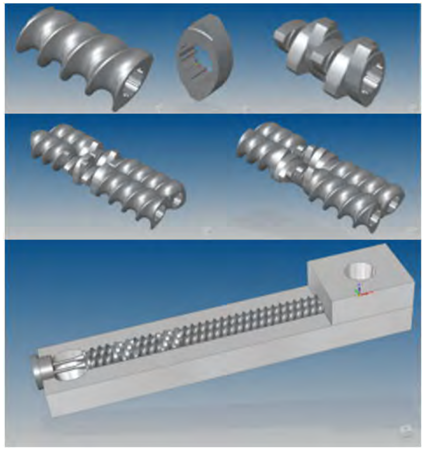
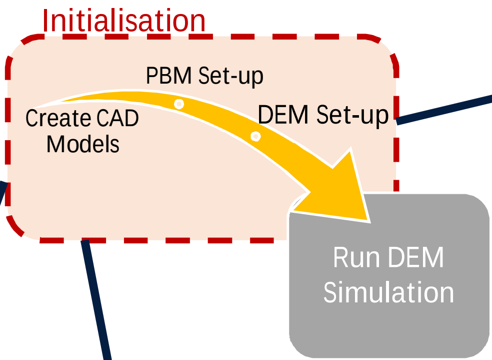
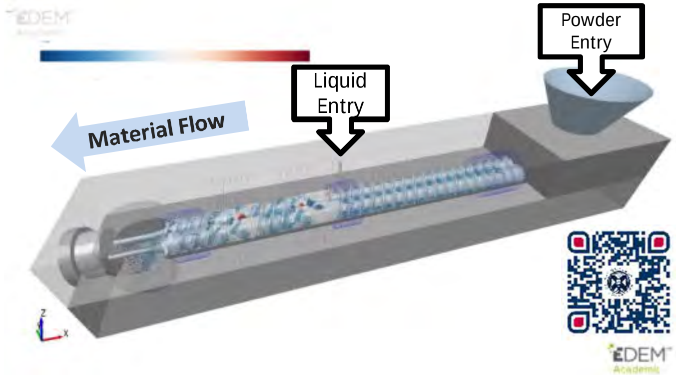
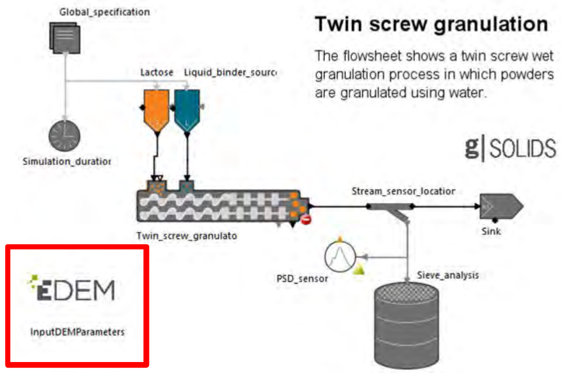
Modelling Cycle









CAD geometries are imported and geometry kinematics are defined.

Particle Size distribution and parameters such as material feed rate and screw speed are imported to the DEM model.

Information such as material properties, class definitions and process parameters are defined in the PBM Flowsheet.

Screw configuration is specified as per the created CAD model.