Formation of the unwanted API agglomerates in the TSG and CMT blenders (WP 4.7)

ADDoPT
ADVANCED DIGITAL DESIGN OF PHARMACEUTICAL THERAPEUTICS

UNIVERSITY OF LEEDS

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Work-Package Objectives

Development of predictive tools for blending processes, using discrete element method (DEM) modelling techniques.

- To determine appropriate particle contact models for the simulations.
- To determine the sensitivity of blending to particles properties and operating conditions.
- To develop a virtual lab whereby the physical and mechanical properties of pharmaceutical powders are calibrated accurately.

Methodology

DEM contact models

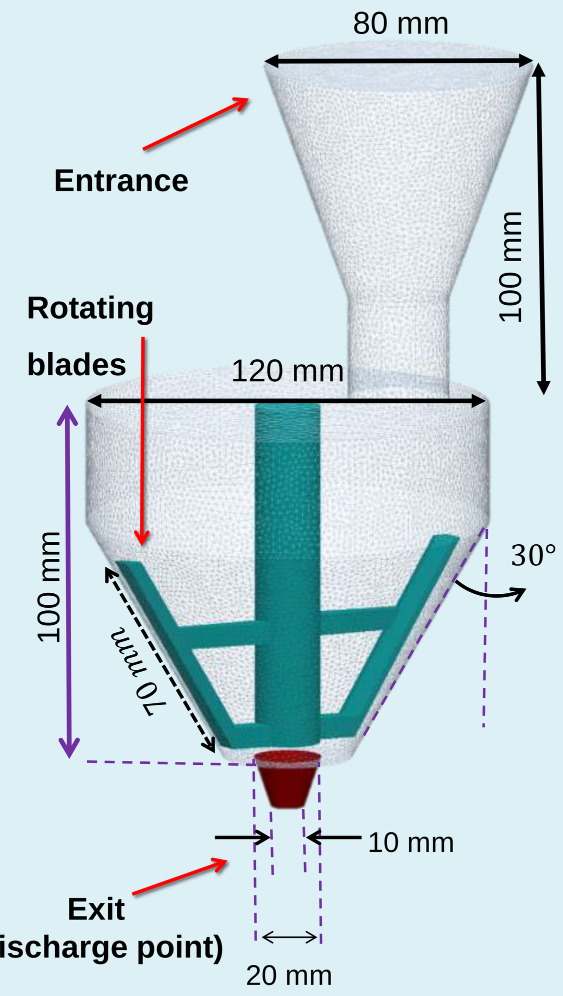
- **Normal/tangential contacts** → Hertz-Mindlin no-slip
- **Cohesion/adhesion effects** → JKR model

CMT and TSG geometries and particles properties

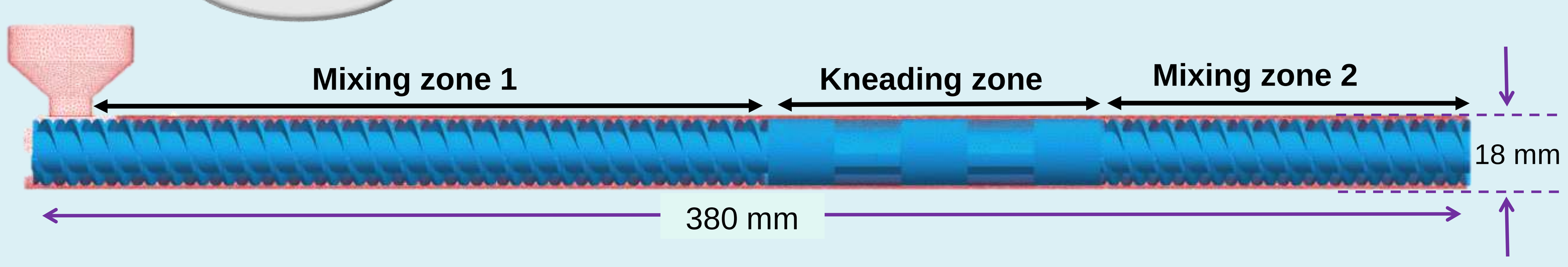
- The geometries and dimensions of the blenders are presented.
- The API and excipient particles are introduced into the blender from the entrance and are mixed by the rotating blade/screw.
- Physical and mechanical properties of the API and excipient particles used in DEM simulations are listed below.

Material	API	Excipient	wall
Particle diameter (μm)	500	1000	-
Density (kg/m3)	1200	1500	7500
Shear modulus (MPa)	100	100	70000
Poisson's ratio	0.25	0.25	0.25
CoR	0.01	0.01	0.01
CoF	0.5	0.5	0.5
Feed rate (kg/s)	0.003	0.030	
Blade rotational speed (rpm)	200		
Interfacial energy (mJm^{-2})	400, 800		
Particle size distribution	Random $0.9\ d \le d_p \le 1.1\ d$		

CMT



TSG



Mixing quantification

Mass fraction $C_{i_k} = \frac{m_{i_k}}{\sum_{i=1}^{n} m_{i_k}}$

Mean value $\mu_i = \frac{1}{n}\sum_{k=1}^{n} C_{i_k}$

Standard deviation $\sigma_i = \sqrt{\frac{1}{n}\sum_{k=1}^{n}\left(C_{i_k} - \mu_i\right)^2}$

Index for segregation

$$RSD_i = \frac{\sigma_i}{\mu_i}$$

Index for *agglomeration*

$$CR_{AA} = \frac{N_{AA}}{N_A} \quad CR_{Ae} = \frac{N_{Ae}}{N_e}$$

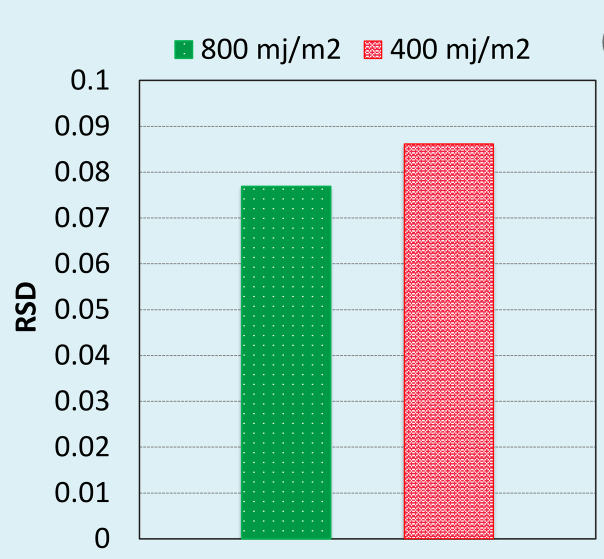
$$CBP = \frac{CR_{Ae}}{CR_{AA}} = \frac{N_{Ae}}{N_{AA}} \cdot \frac{N_A}{N_e}$$

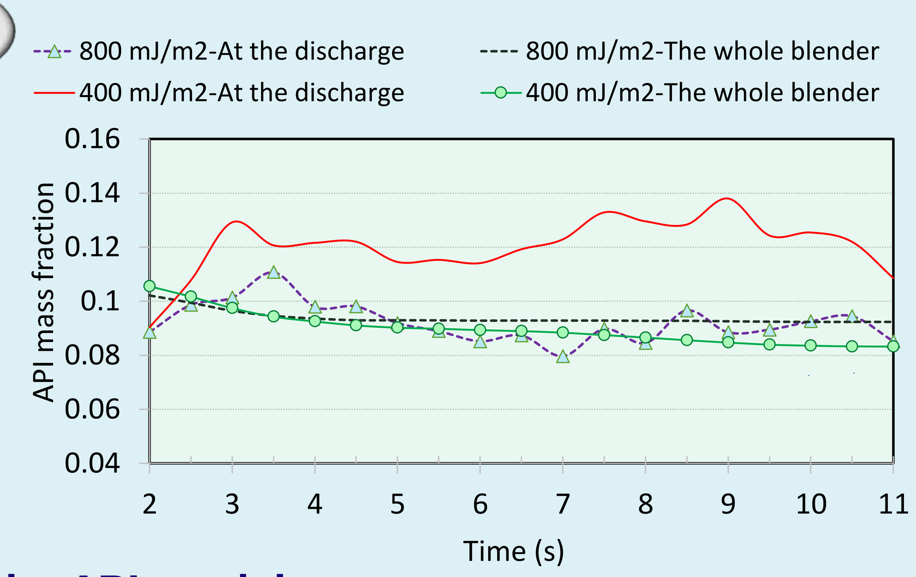
Simulation results

Effect of surface energy on APIs mass fraction

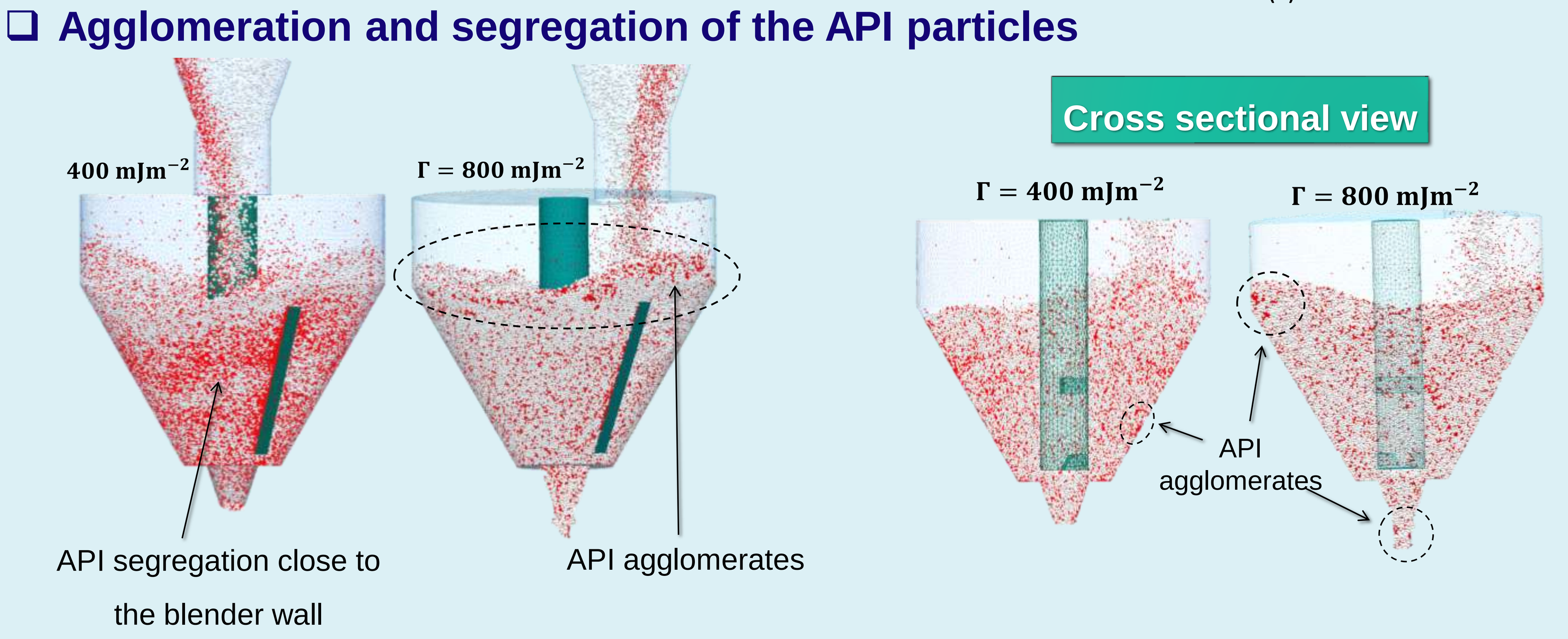
- The API particles mass fraction at the exit and inside the blender are presented.
- The API mass fraction shows fluctuations at the discharge point.
- Increasing the particles surface energy has reduced the mass fraction variations significantly.

CMT



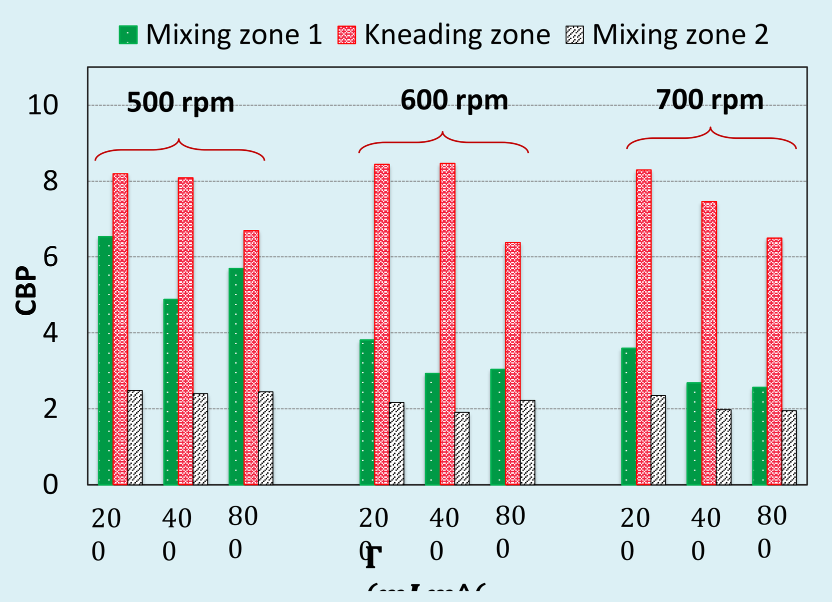


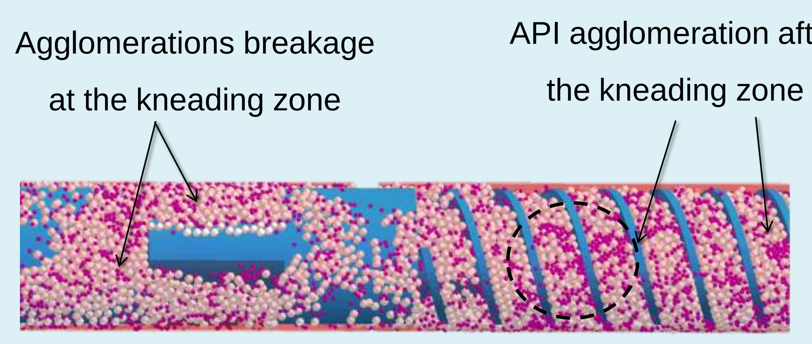
Agglomeration and segregation of the API particles



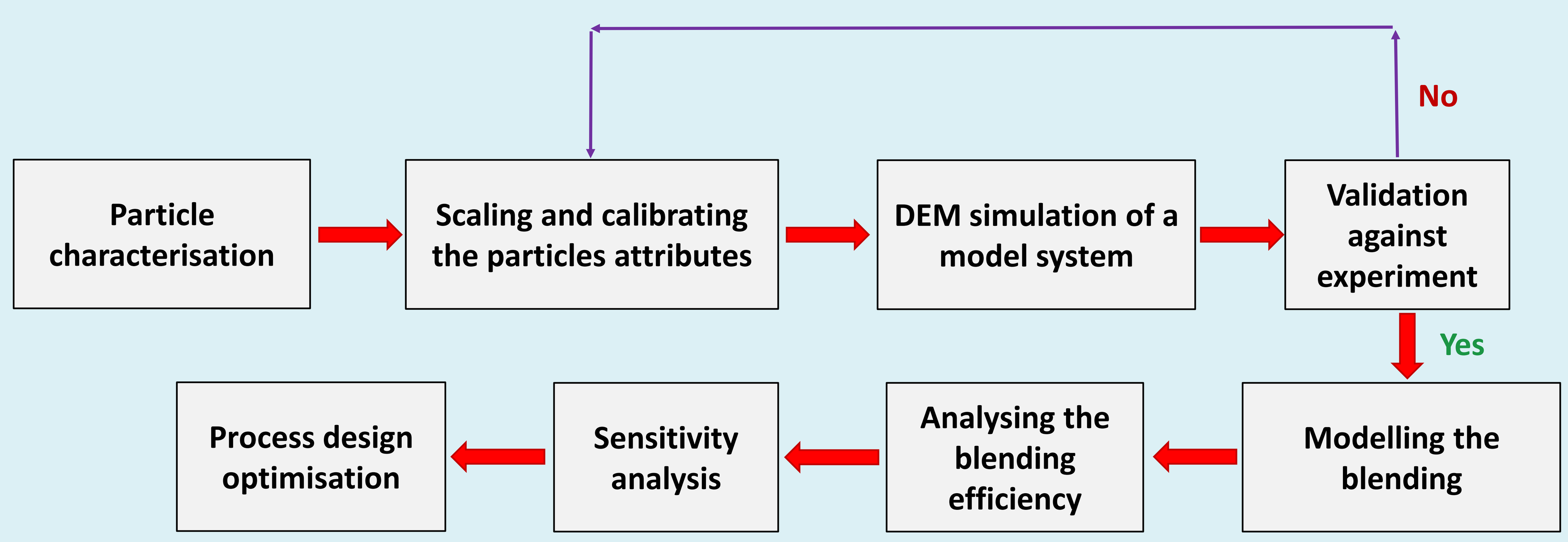
Segregation of the APIs close to the blender wall is very likely when particles are not highly cohesive.

TSG





Work flow for predicting the efficiency of the blending



References

[1] Johnson, K. L., K. Kendall, and A. D. Roberts. "Surface energy and the contact of elastic solids." *Proceedings of the Royal Society of London A: Mathematical, Physical and Engineering Sciences*. Vol. 324. No. 1558. The Royal Society, 1971.

[2] Thornton, Colin, and Zemin Ning. "A theoretical model for the stick/bounce behaviour of adhesive, elastic-plastic spheres." *Powder technology* 99.2 (1998): 154-162.

[3] *Behjani, Mohammadreza Alizadeh, Nejat Rahmanian, and Ali Hassanpour. "An investigation on process of seeded granulation in a continuous drum granulator using DEM." *Advanced Powder Technology* (2017).

ADDoPT is a collaboration instigated by the Medicines Manufacturing Industry Partnership, and part funded under the Advanced Manufacturing Supply Chain Initiative, a BEIS initiative delivered by Finance Birmingham and Birmingham City Council.

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