One dimensional model for the prediction of residence time distribution during twin-screw granulation

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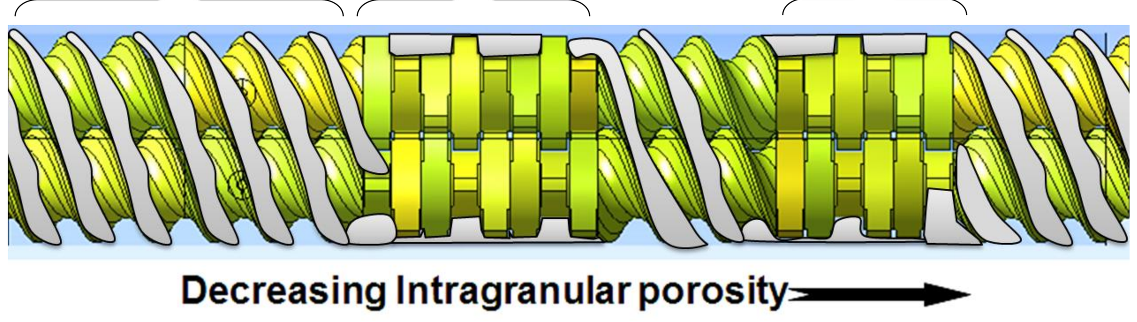
Introduction

- Continuous wet granulation performed using twin-screw granulators (TSG) is an important part of future continuous manufacturing of pharmaceutical solid dosage forms.
- The extent of different rate processes such as wetting, growth and breakage involved in granulation are greatly governed by the residence time distribution within each module where individual rate processes dominate over others.
- Currently, visual observations and experimental data are used to determine the residence time distributions (RTD).
- In this study, a dynamic transport model was developed based on classical chemical engineering methods.

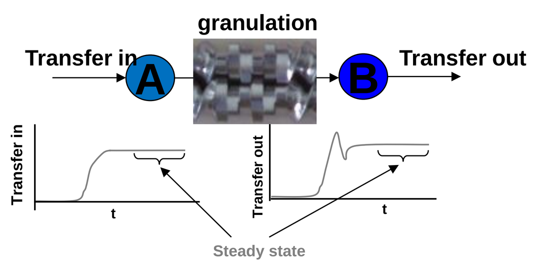
Continuous high shear wet granulator

System at steady-state



- Dynamics are transient
- At appropriate time-scales and conditions, granulation is in steady state
- Two key implications

1. Fluxes are roughly constant
2. Internal concentrations are constant.



transfer in ≈ constant ≈ transfer out

$$\frac{d[P_m]}{dt} \approx 0 \approx \frac{d[G_m]}{dt}$$

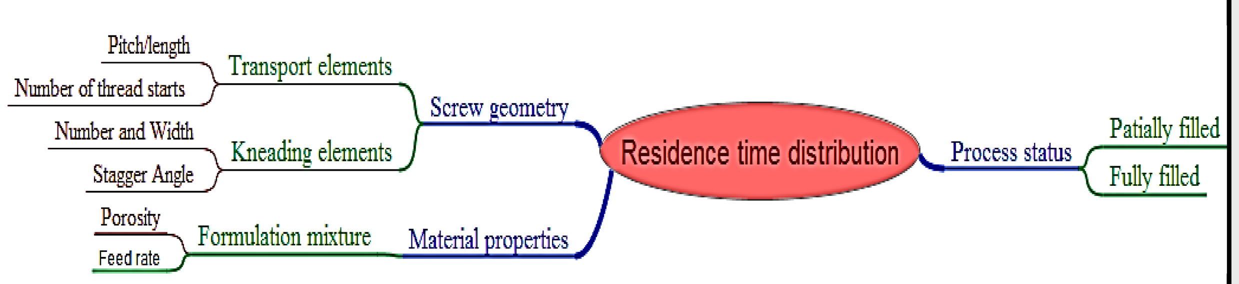
Why RTD is needed?

For a section of the TSG which can be safely assumed to be well-mixed at steady state with representative overflow, the population balance simplifies as:

$$0 = \dot{Q}_{ex}(n_{in}(x) - n(x)) - VG\frac{\partial n(x,t)}{\partial x} + V\dot{b}(x) - V\dot{d}(x)$$

$$\Rightarrow G\frac{dn(x,t)}{dx} = \frac{1}{\tau}(n_{in}(x) - n(x)) + \dot{b}(x) - \dot{d}(x) \text{ where } \tau = \frac{V}{\dot{Q}_{ex}}$$

Factors affecting RTD

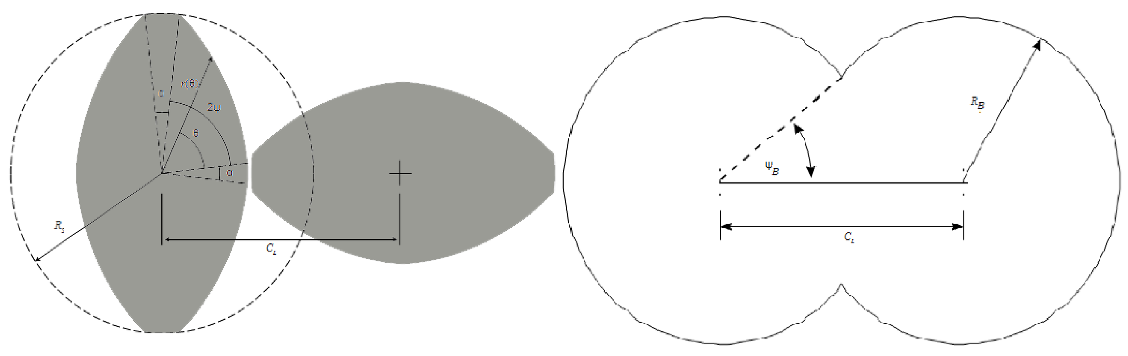


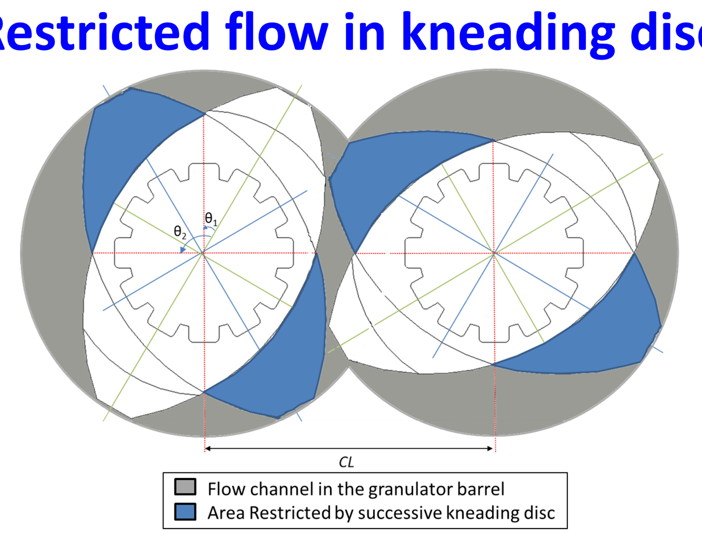
Modelling approach

Unrestricted flow in transport screw

Restricted flow in kneading disc

$$V_c = (n_s S + n_k K_d)(A_{bx} - 2A_{sx})$$





$$A_{sx} = n_t(\psi_s C_L^2 - C_L R_S \sin\psi_s) + \frac{1}{2}n_t\alpha[R_S^2 + (C_L - R_S)^2$$

$$A_{bx} = 2(\pi - \psi_B)R_b^2 + C_L R_B \sin\psi_B$$

$$A_{res} = A_{sx} - A_{overlap} \quad \text{where,}$$

$$A_{overlap} = 4\frac{R_s}{R_r}\frac{\tan^{-1}\left(\frac{Rr}{Rs}\tan\theta_1\right) - \tan^{-1}\left(\frac{Rr}{Rs}\tan\theta_2\right)}{2}\left(\frac{R_s}{2}\right)^2$$

Partially filled zone

$$R_{fill_i} = \frac{Q_{fr_i}}{Q}$$

Fully filled zone

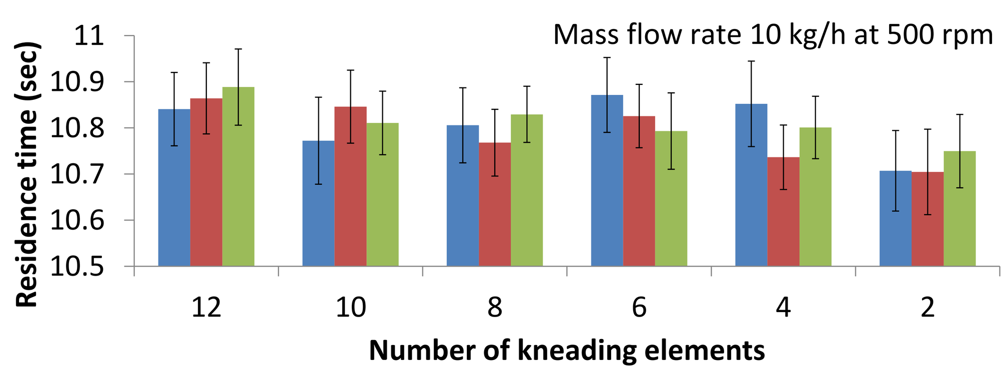
$$R_{fill_i} = \frac{Q_{fr_i}}{v_{k_z}(A_{bx} - 2A_{sx})}$$

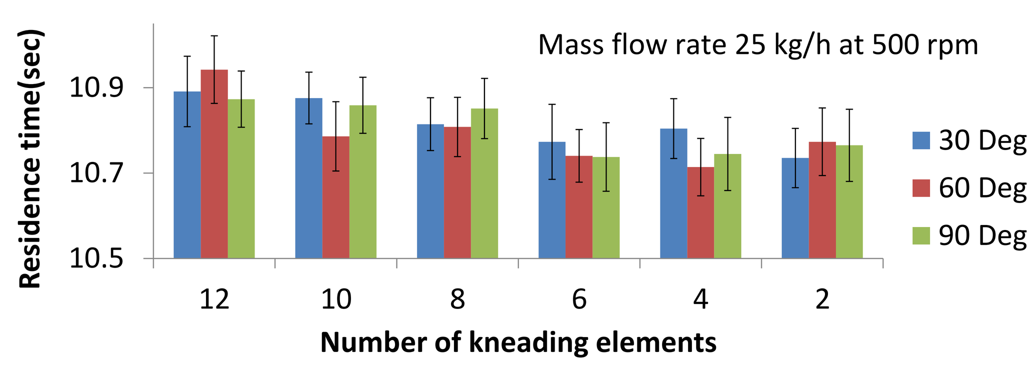
$$\tau_i = \frac{(A_{bx} - 2A_{sx})_i \delta L R_{fill\,i}}{Q_{fr\,i}}$$

$$\tau_{tot} = \sum_{pfz}\tau_{partially-filled} + \sum_{fz}\tau_{fully-filled}$$

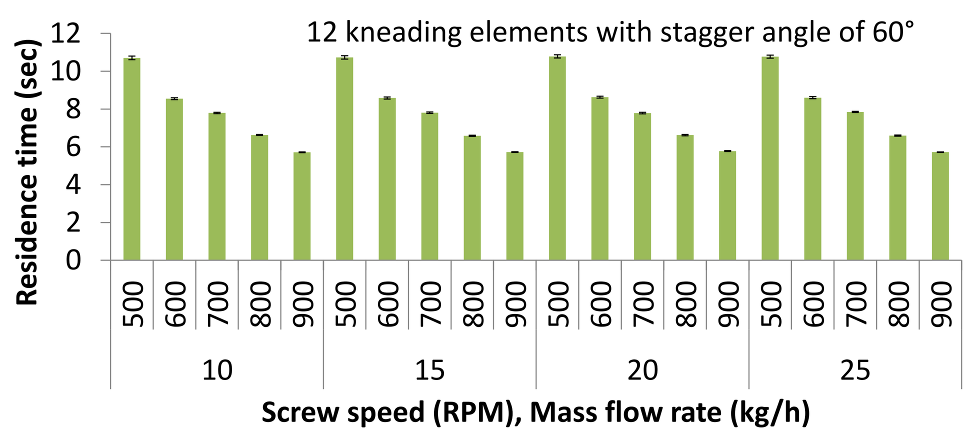
- Along with the throughput, restriction to the material flow dictate the fill level in the various sections of the TSG.
- Monte Carlo simulation: Simulations were performed making use of internally generated (pseudo) random numbers, randomly distributing the fluctuations/disturbance caused by un-assigned model parameters (back pressure, leakage flow etc.) on parameters implemented in the design equations (filling degree) given above to observe the effect of change in equipment and process design parameters on RTD.

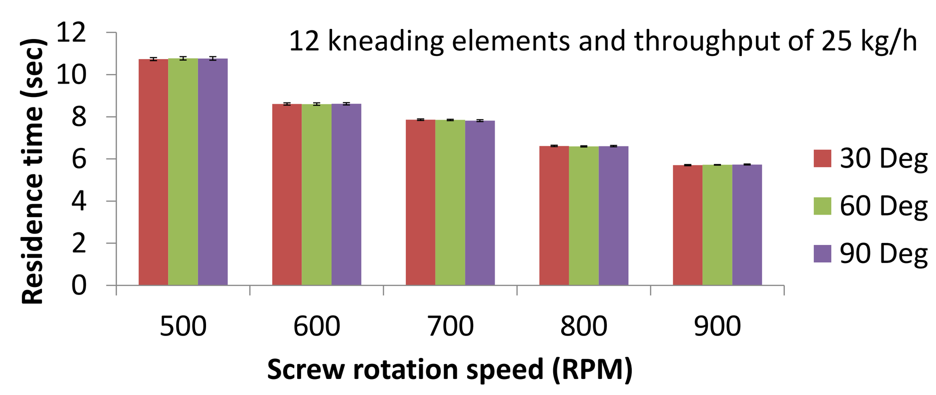
Simulation results:





RTD of material equally governed by the throughput and stagger angle when screw rotation speed is constant.





Compared with screw rotation speed , the throughput and stagger angle almost had no impact on the RTD of TSG.

Conclusions:

- The study provides a theoretical transport model and predict RTD which can be later coupled with a population balance model in order to predict more realistic granulation yields in a TSG.
- The partially filled zone, act more as a drag pump, and therefore the residence time is largely governed by the screw speed. However for a constant screw speed other parameters such as process throughput, stagger angle and number of kneading elements come into play.
- More the kneading elements added to the screw configuration, longer the mean residence time in the TSG due to the high restriction to the flow caused by the increased number of kneading disc.
- Experimental validation of theoretical model should be the next step to get better insight on RTD .

Acknowledgments

Financial support for this research from the BOF (Bijzonder Onderzoeksfonds Universiteit Gent, Research Fund Ghent University) is gratefully acknowledged.

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