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Model-based analysis and experimental validation of residence time distribution in twin-screw granulation

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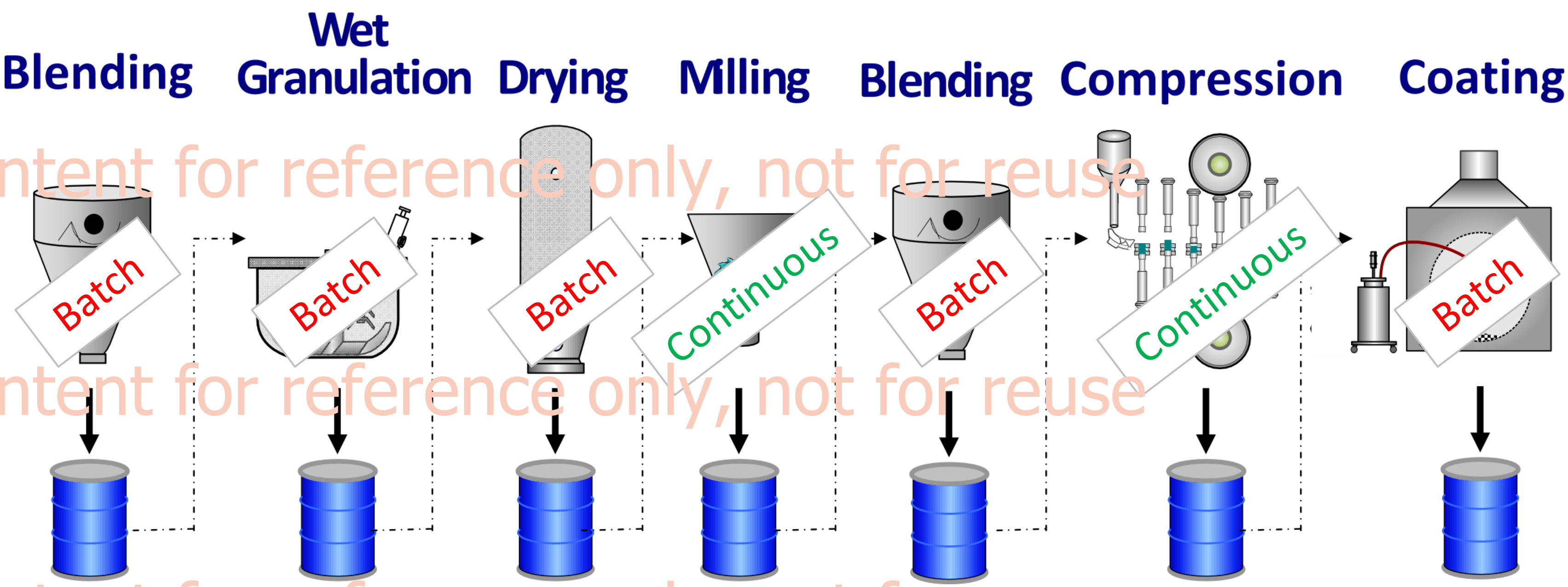
Current solid-dosage manufacturing is slow and expensive

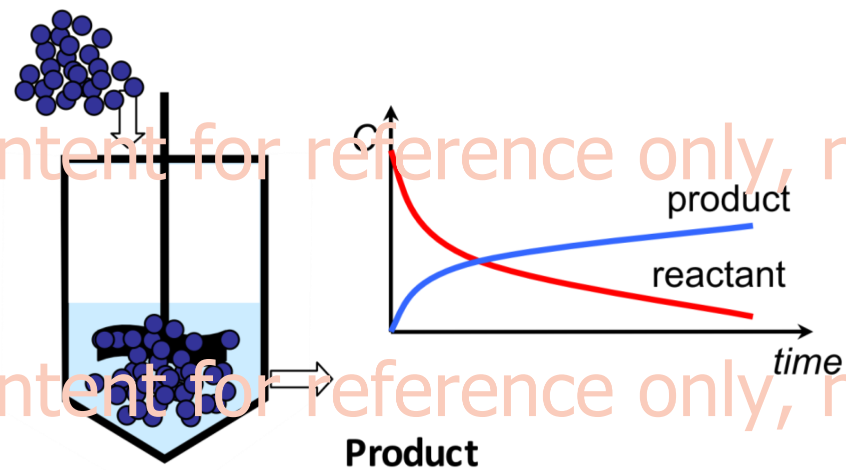


Product collected after each unit operation

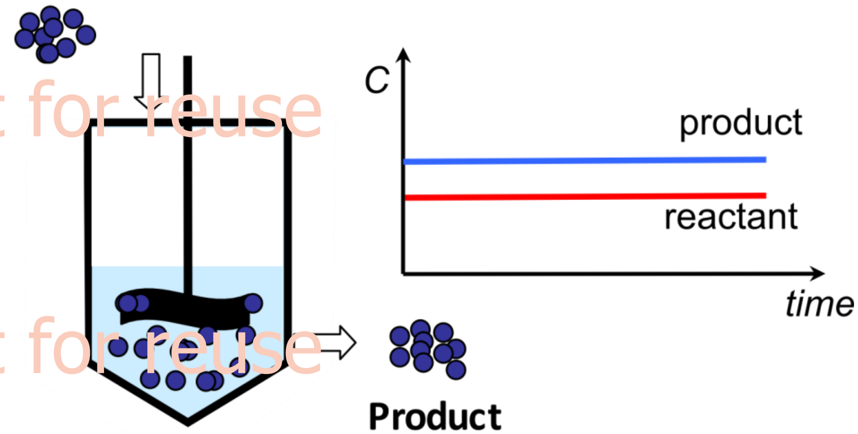
Actual processing time = days to weeks

Continuous manufacturing is better

Batch



Continuous



Batch

- ✘ No feed and effluent
- ✘ Concentration is time variant
- ✘ High variability
- ✓ Process control is easy

Continuous

- ✓ Constant feed and effluent
- ✓ Concentration are constant
- ✓ Low variability
- ✘ Rigorous control required

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Continuous manufacturing line

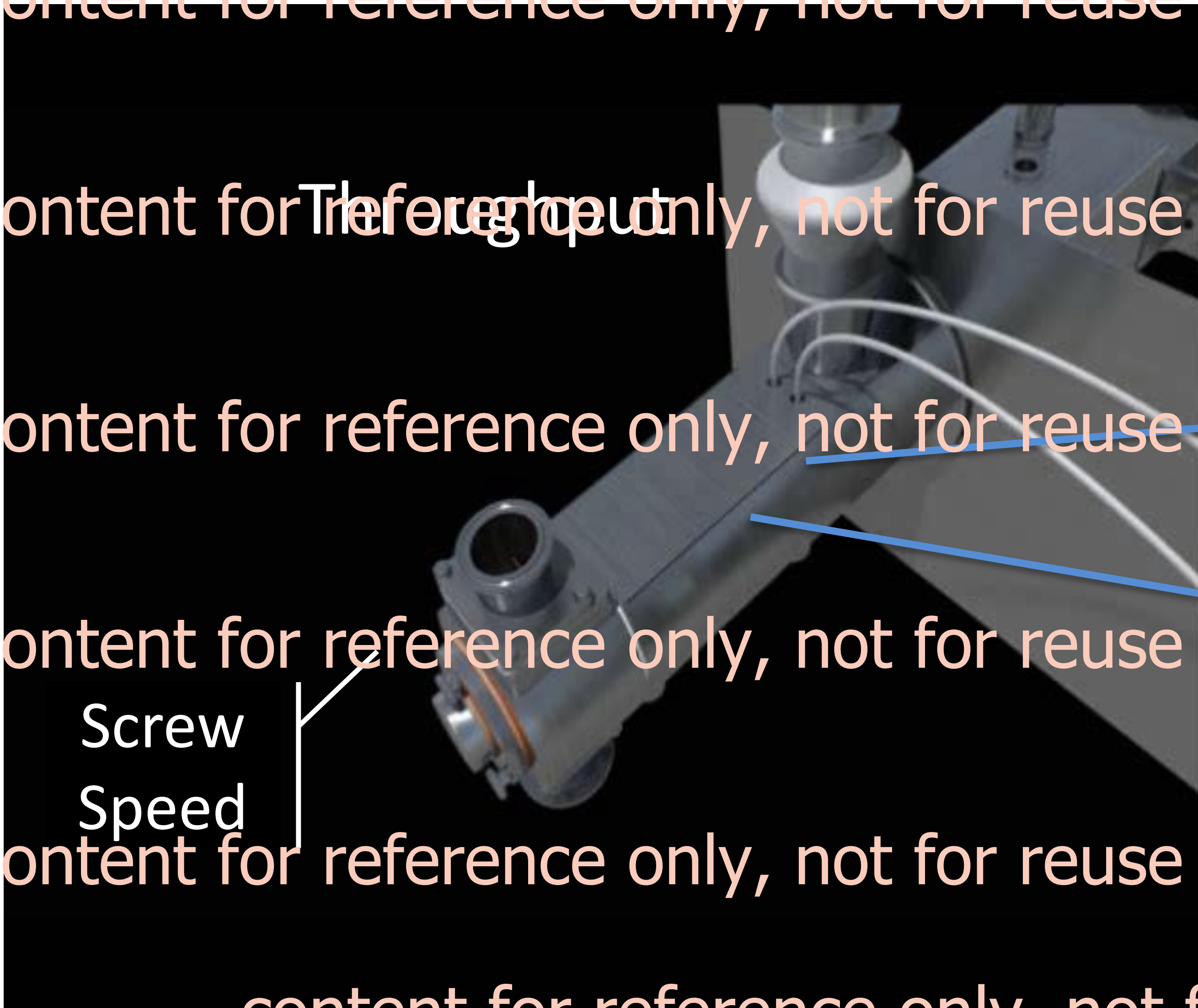
Consigma™-25 system

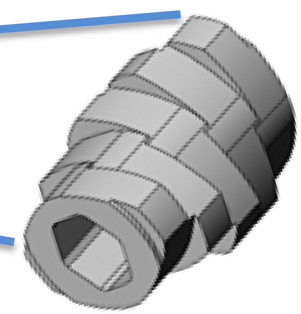
Continuous twin-screw granulator

Segmented Fluid bed dryer

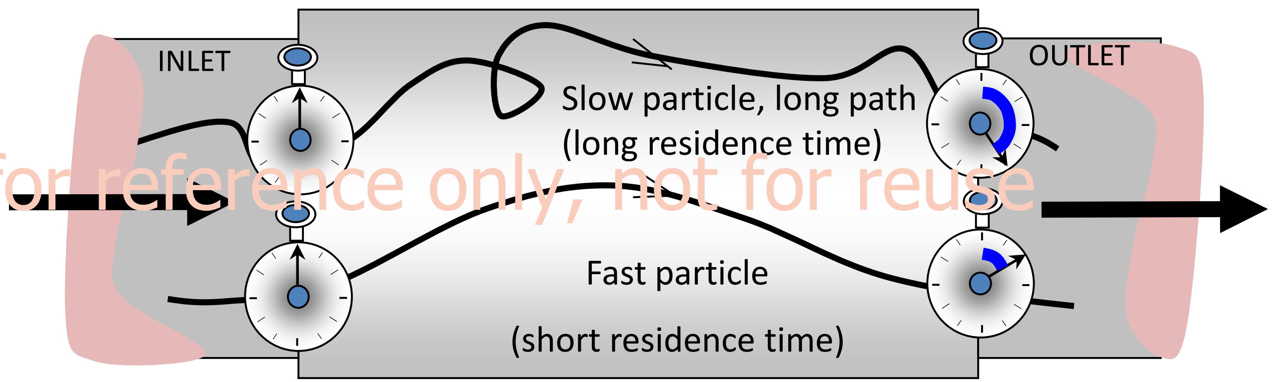
Granule conditioning module

Design of granulator screw, screw speed, material feed rate control granulation





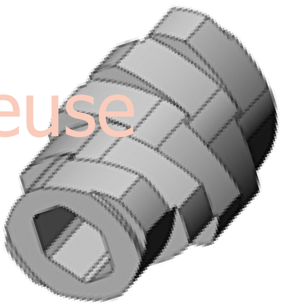
Residence time distribution to know the granulation time and mixing



Residence time distribution to know the granulation time and mixing

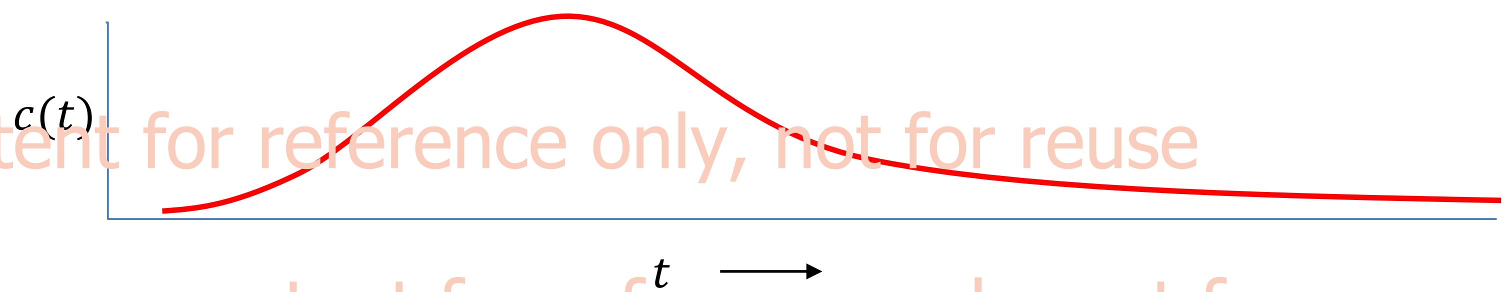
Screw Configuration

- Number of kneading discs
- Stagger angle



Process parameters

- Material throughput
- Screw speed



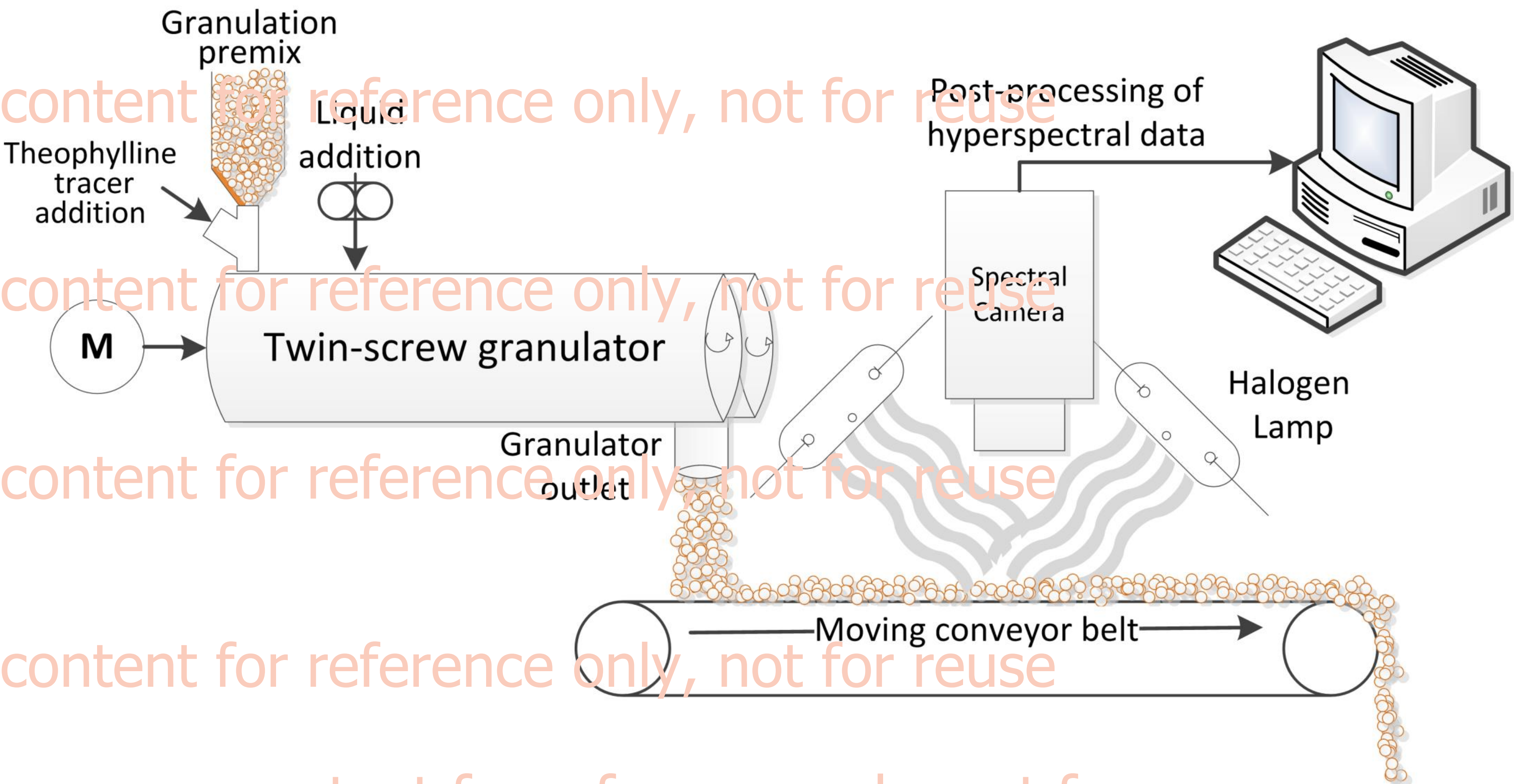
Analysis of residence time distribution in twin-screw granulation

RTD Measurement by Chemical Imaging

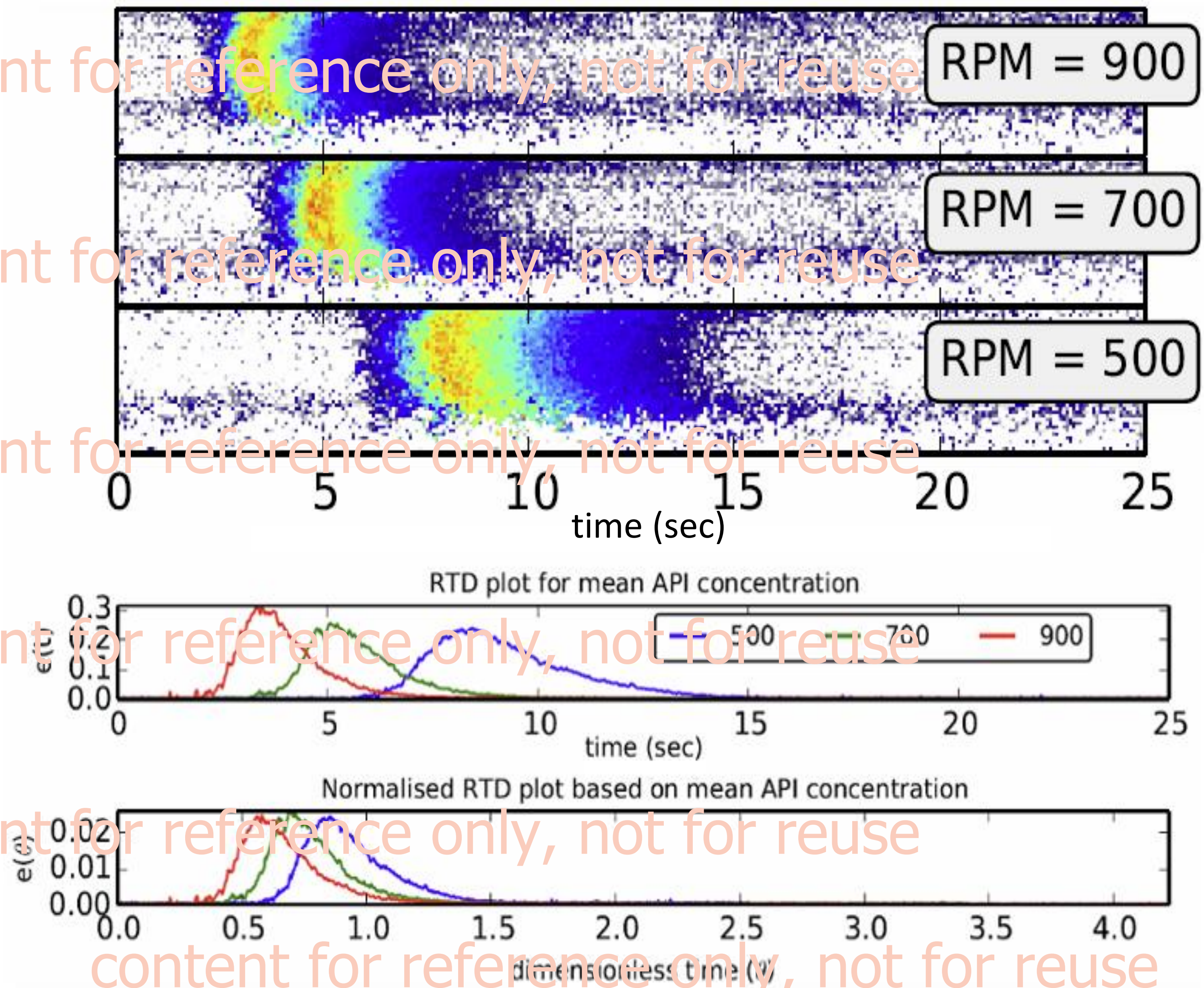
Model Formulation

Outcomes

Tracer concentration in granules produced was measured using NIR chemical imaging



API Map was used to measure RTD



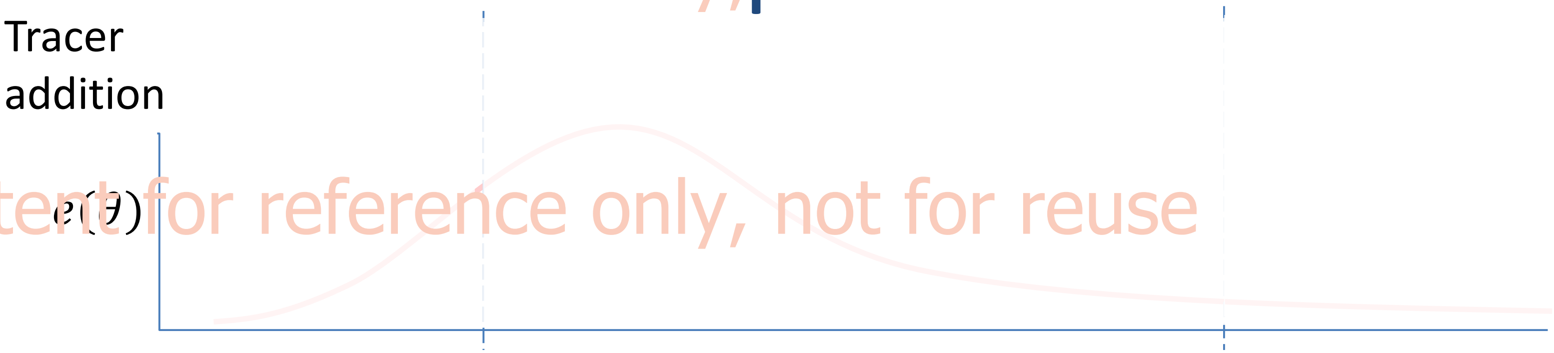
Analysis of residence time distribution in twin-screw granulation

RTD Measurement by Chemical Imaging

Model Formulation

Outcomes

Conceptual model to include three main components of RTD

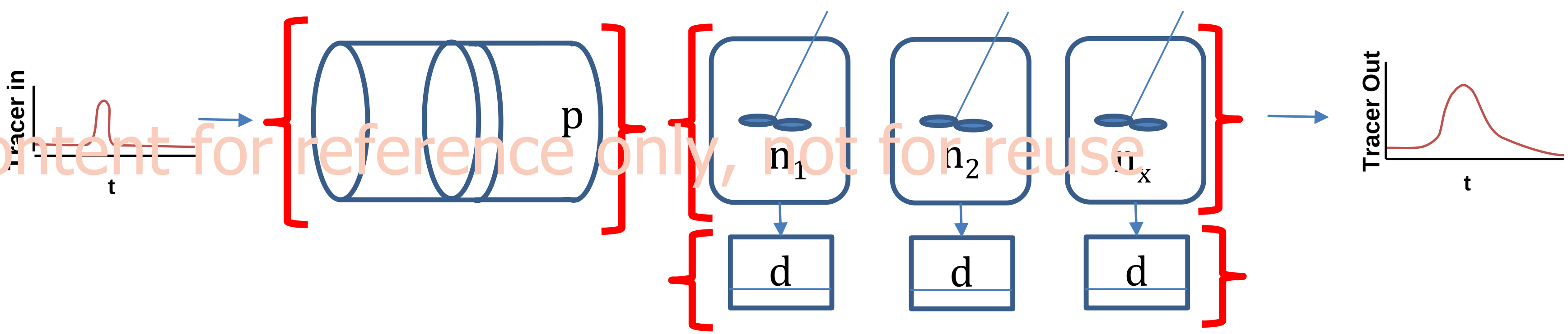


Modified Tank-in-Series model used

Modified Tank-In-Series model

$$e(\theta) = \frac{b[b(\theta - p)]^{n-1}}{(n-1)!} exp^{[-b(\theta-p)]}$$

where, $b = \frac{n}{(1-p)(1-d)}$



Source: Levenspiel, Chemical Reaction Engineering, 1999

Analysis of residence time distribution in twin-screw granulation

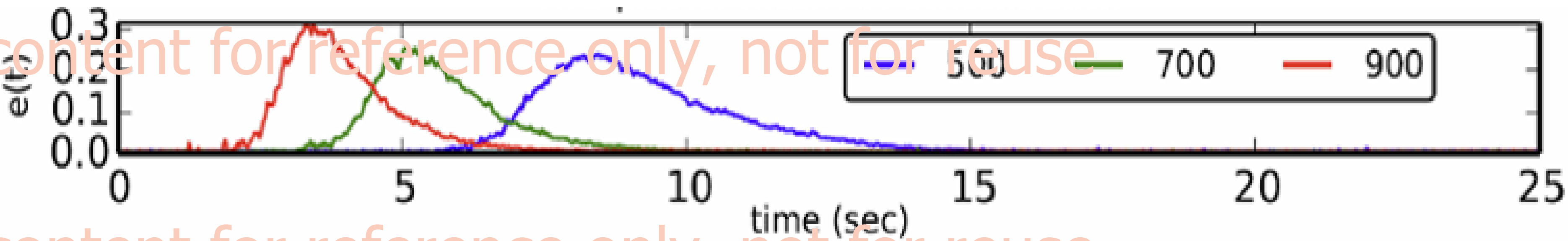
RTD measurement by Chemical imaging

Model Formulation

Outcomes

Measurement based
- Mean residence time
- Mean centred variance

Model based
- Number of CSTR
- Plug flow fraction
- Dead volume fraction



$$\tau = \frac{\int_0^\infty t \cdot e(t)dt}{\int_0^\infty e(t)dt}$$

Mean residence time , τ

(a measure of the mean of the distribution)

$$\sigma^2 = \frac{\int_0^\infty (t-\tau)^2 \cdot e(t)dt}{\int_0^\infty e(t)dt}$$

Variance, σ^2

(width of the distribution)

Analysis of residence time distribution in twin-screw granulation

Chemical imaging based RTD measurement

Model Formulation

Outcomes

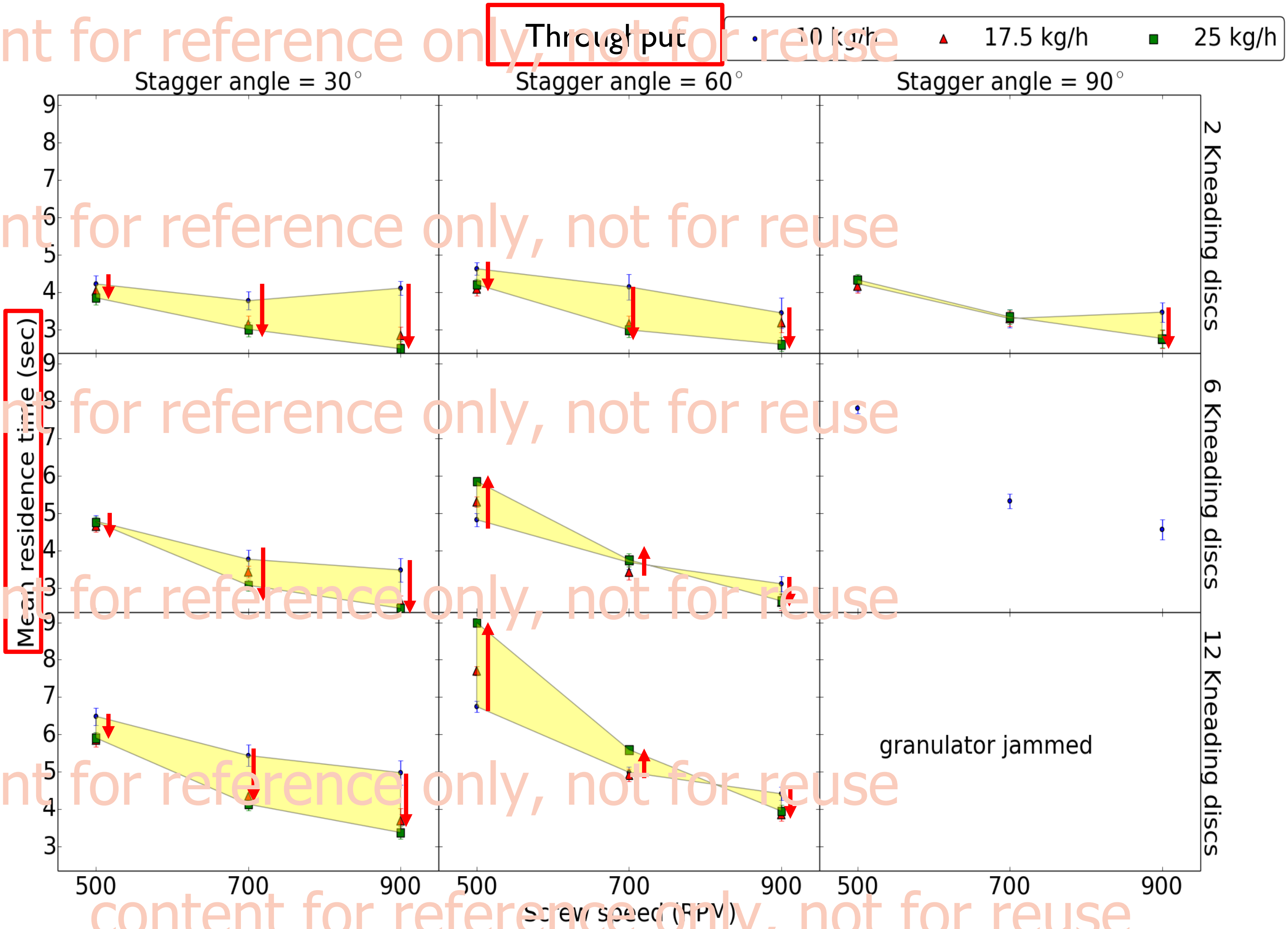
Measurement based
- Mean residence time
- Mean centred variance

Model based
- Number of CSTR
- Plug flow fraction
- Dead volume fraction

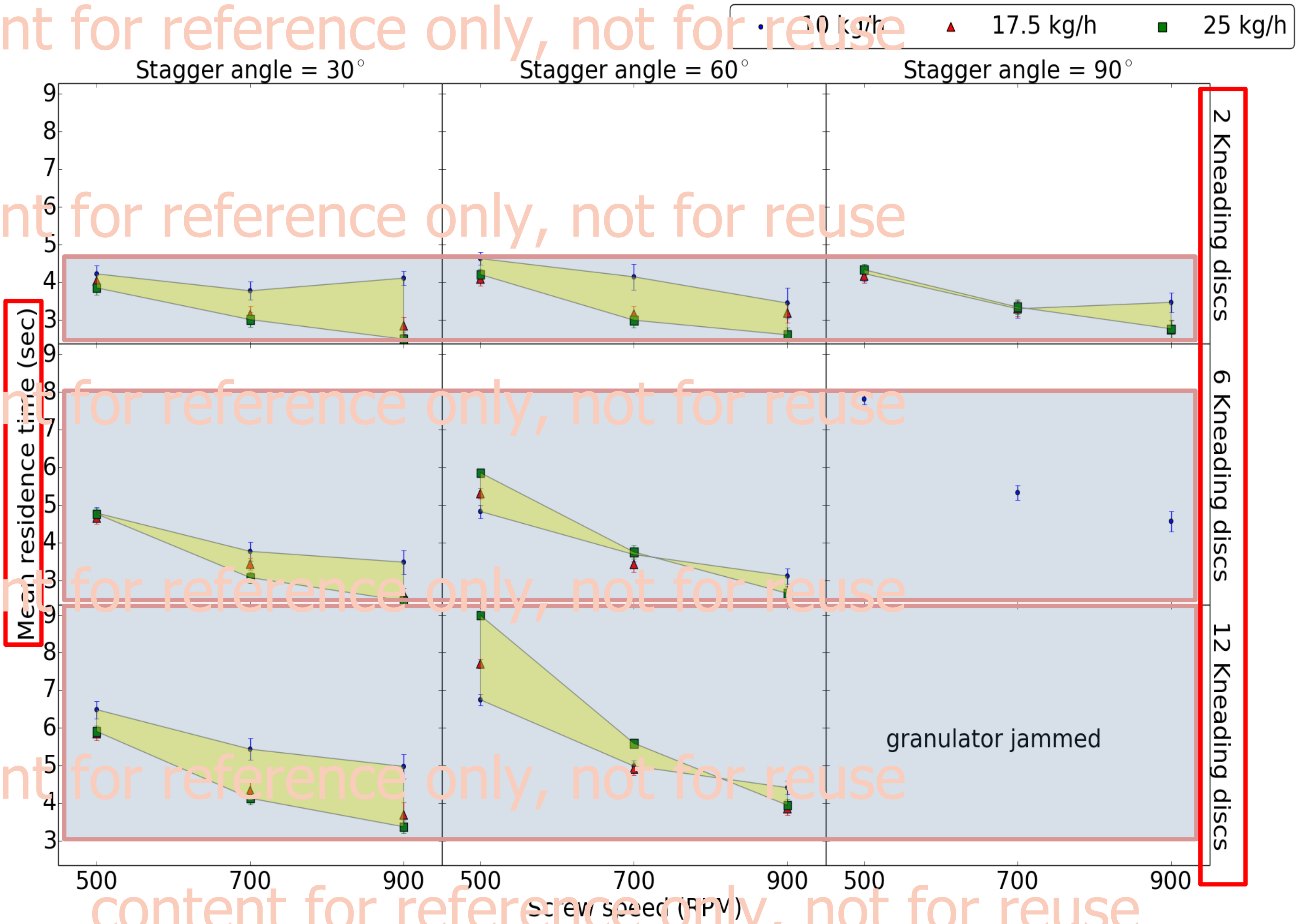
Residence time reduces with increase in screw speed

Measure of the mean of the distribution

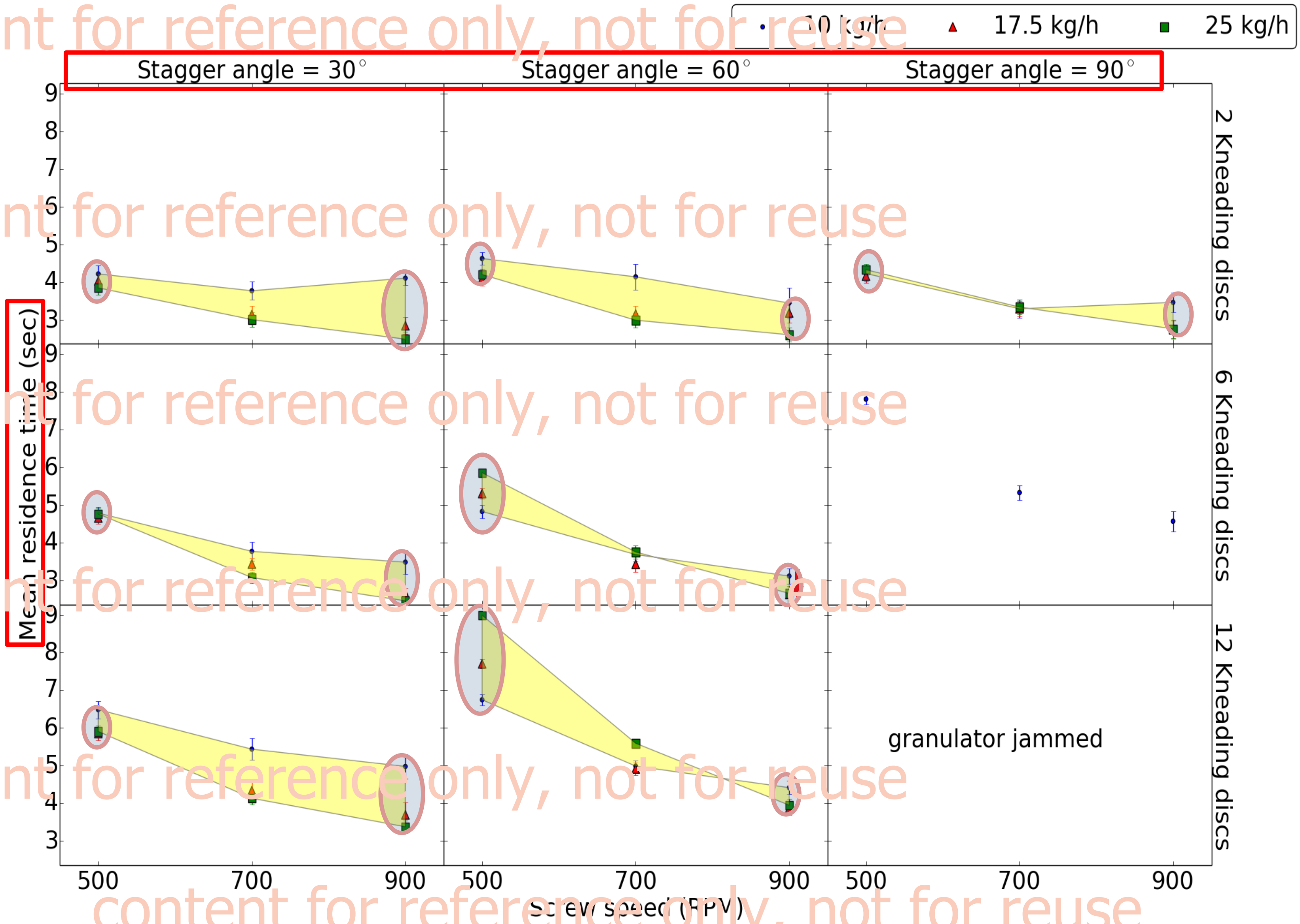
Residence time reduces with increase in throughput...but not always



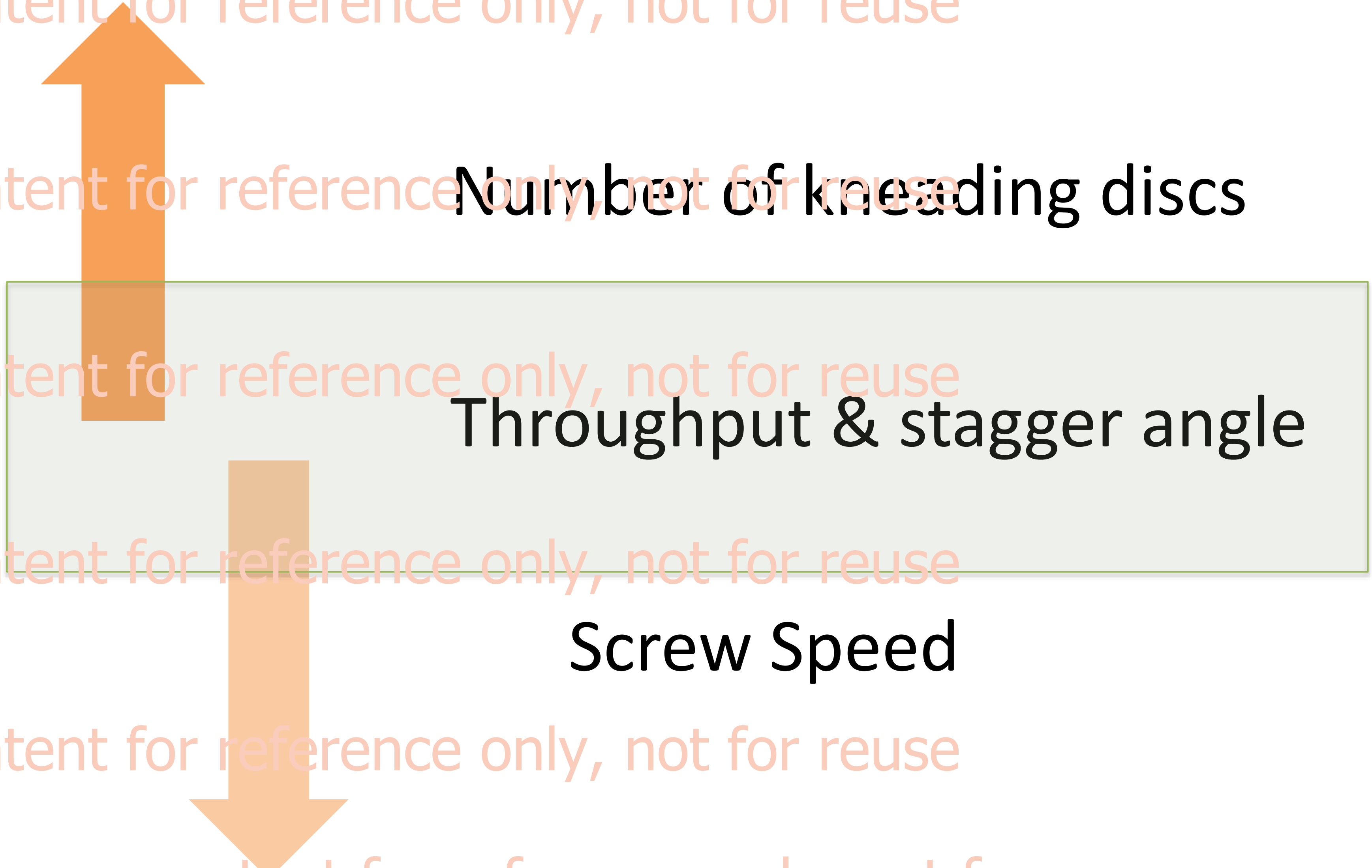
Residence time increases with increase in number of kneading discs.



Residence time reduces with increase in stagger angle.



Mean of the residence time distribution



Analysis of residence time distribution in twin-screw granulation

Chemical imaging based RTD measurement

Model Formulation

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Measurement based
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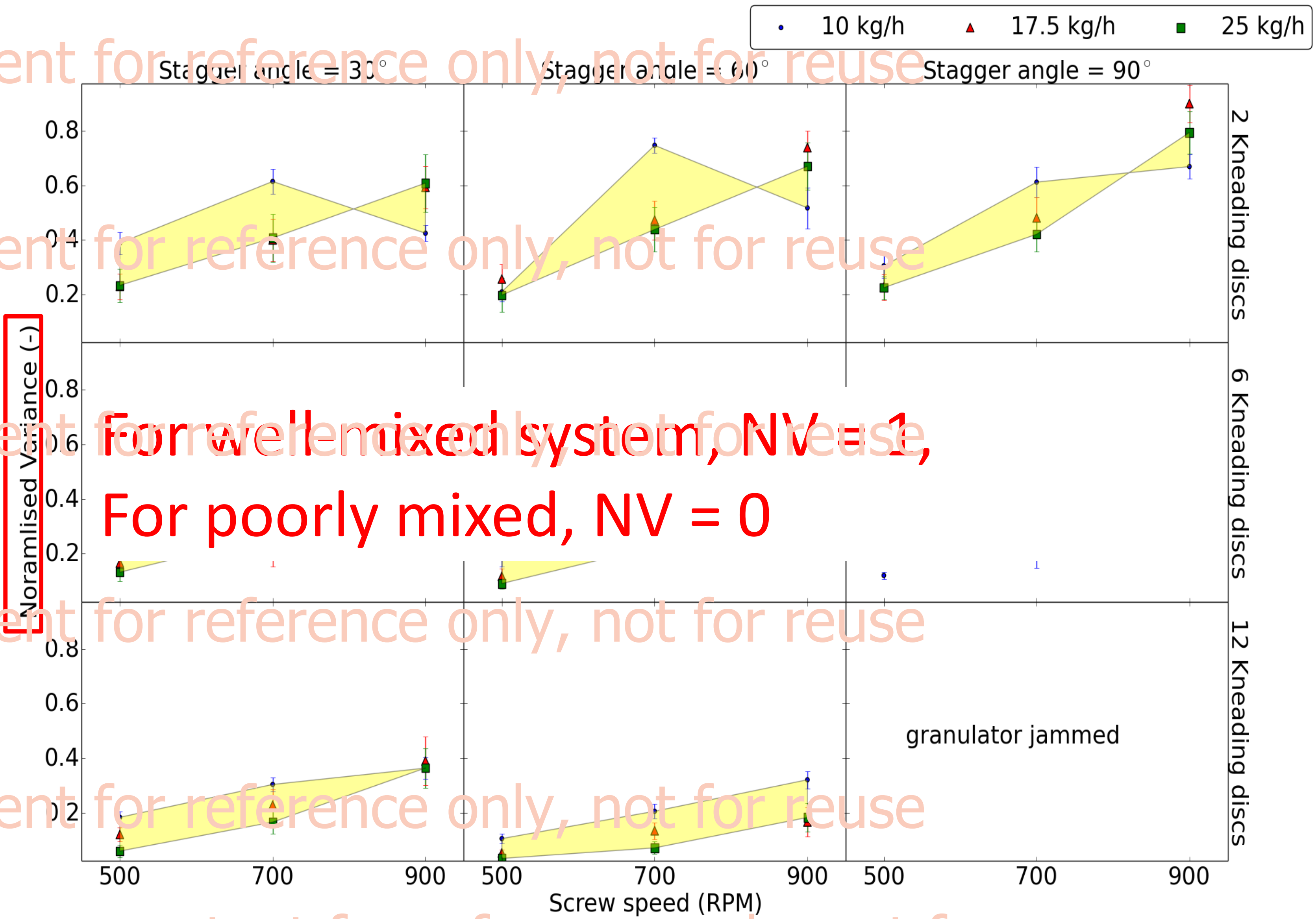
- Mean centred variance

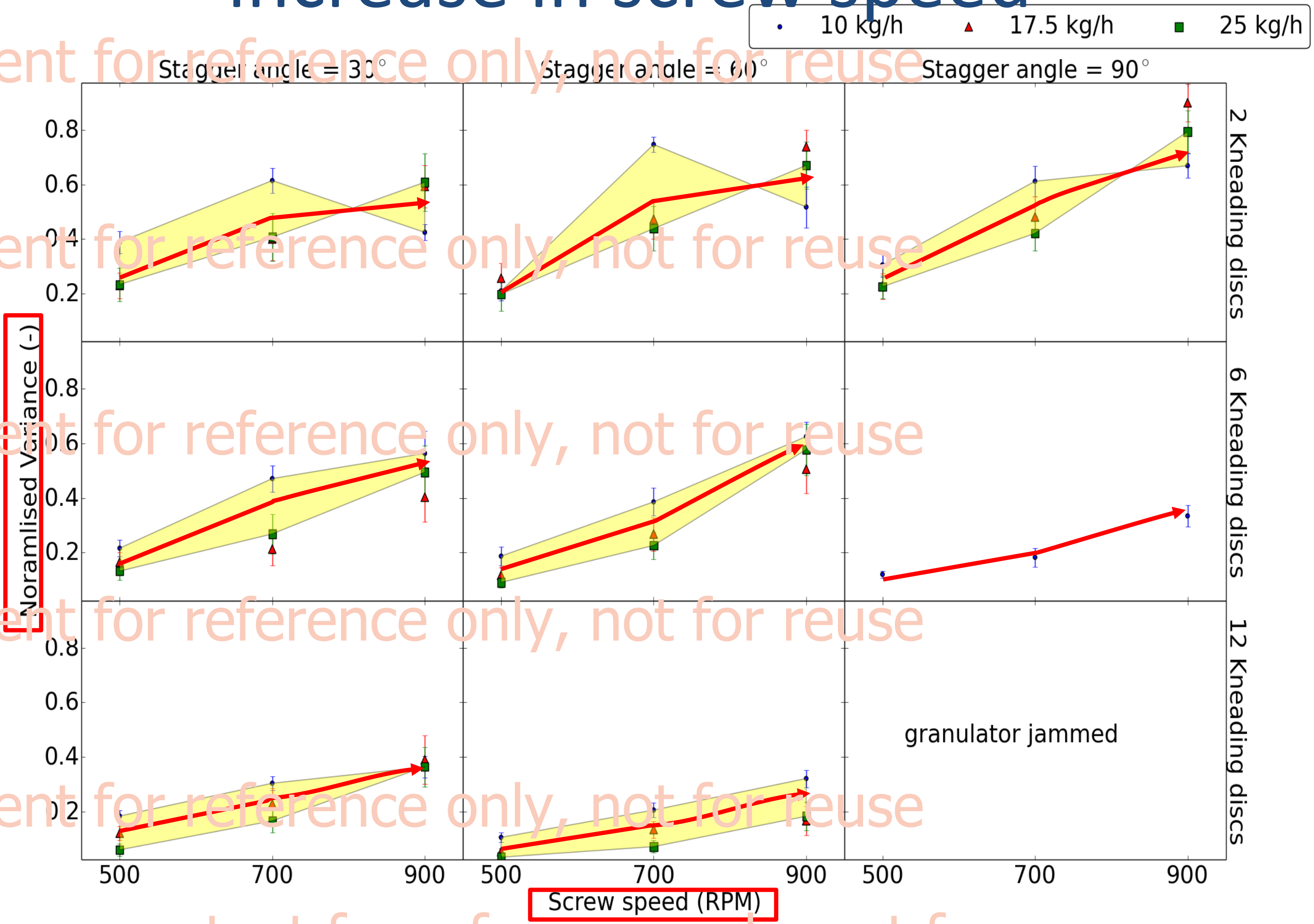
Model based
- Number of CSTR
- Plug flow fraction
- Dead volume fraction

Width of the distribution shows axial mixing

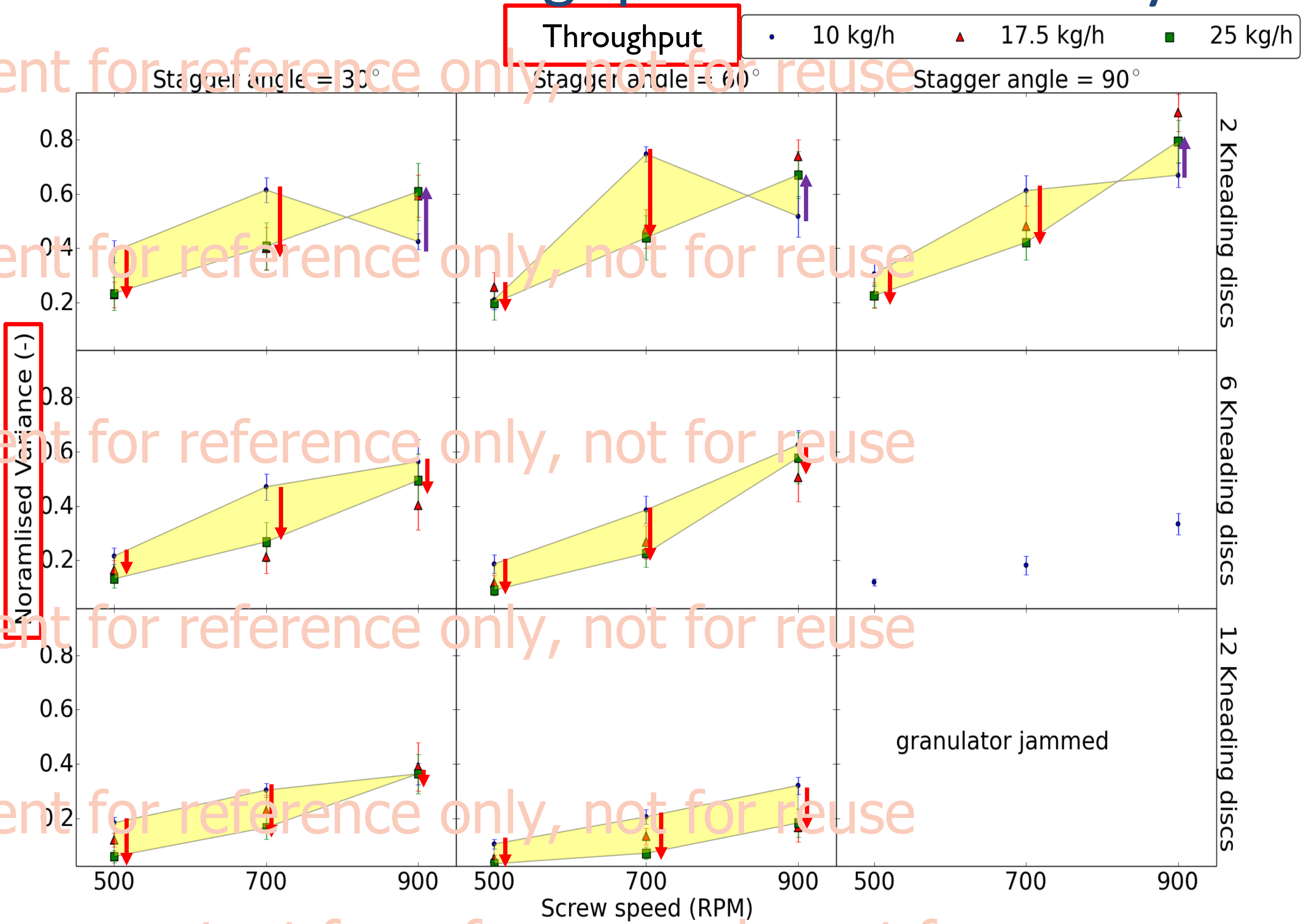


For well-mixed system, NV = 1,
For poorly mixed, NV = 0

Axial mixing increases with increase in screw speed

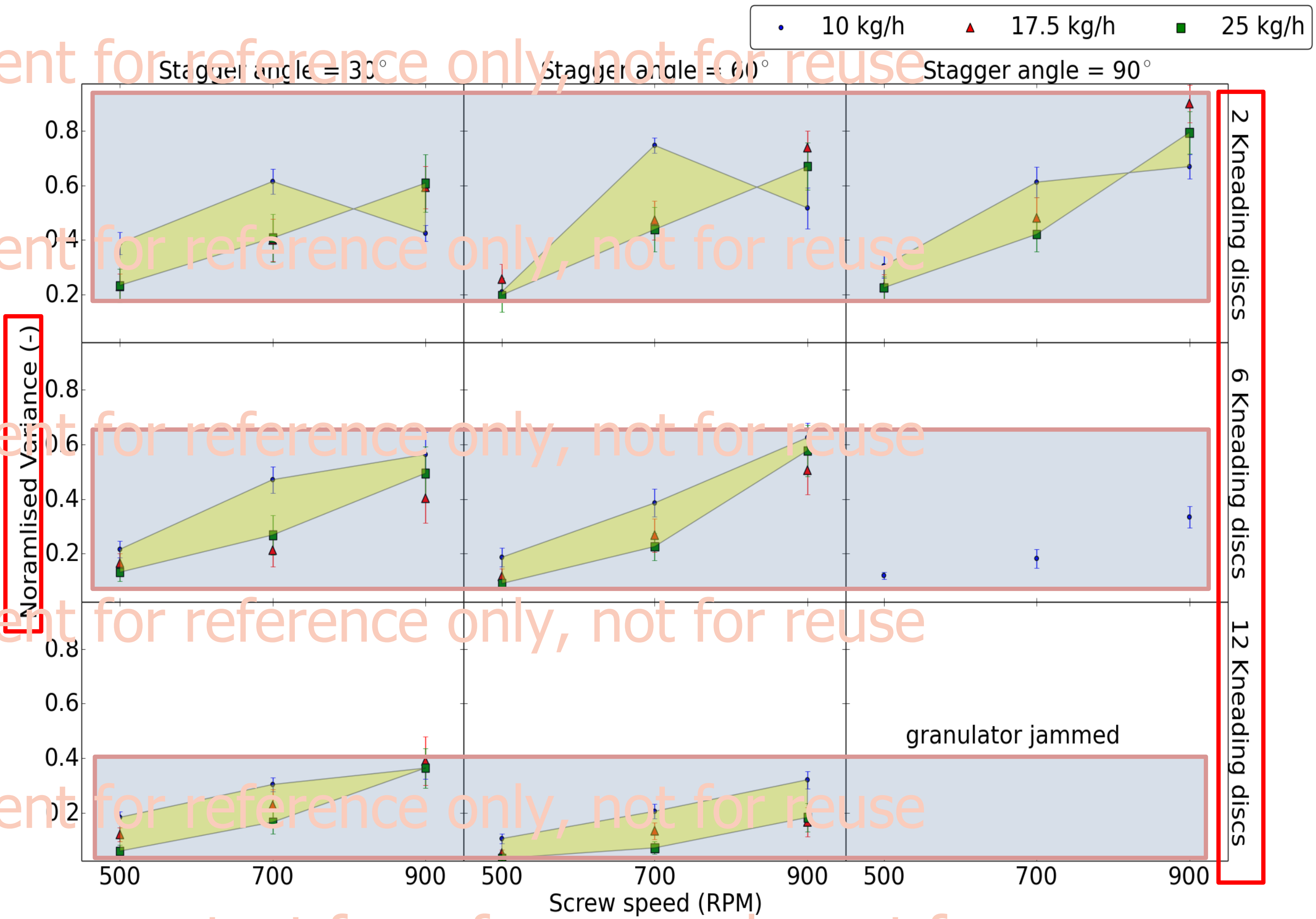


Axial mixing increases with increase in throughput…but not always



For well-mixed system NV = 0, For poorly mixed NV = 0

Axial mixing decreases with increase in number of kneading discs



Increase in stagger angle caused reduction in axial mixing

For well-mixed system NV = 1, For poorly mixed NV = 0

Major factors had opposite effects on residence time and axial mixing

Factors	Residence time	Axial Mixing
Number of kneading discs	Increase	Decrease
Screw Speed	Decrease	Increase
Throughput	Interaction	Interaction
Stagger angle	interaction	Interaction

Analysis of residence time distribution in twin-screw granulation

Chemical imaging based RTD measurement

Model Formulation

Outcomes

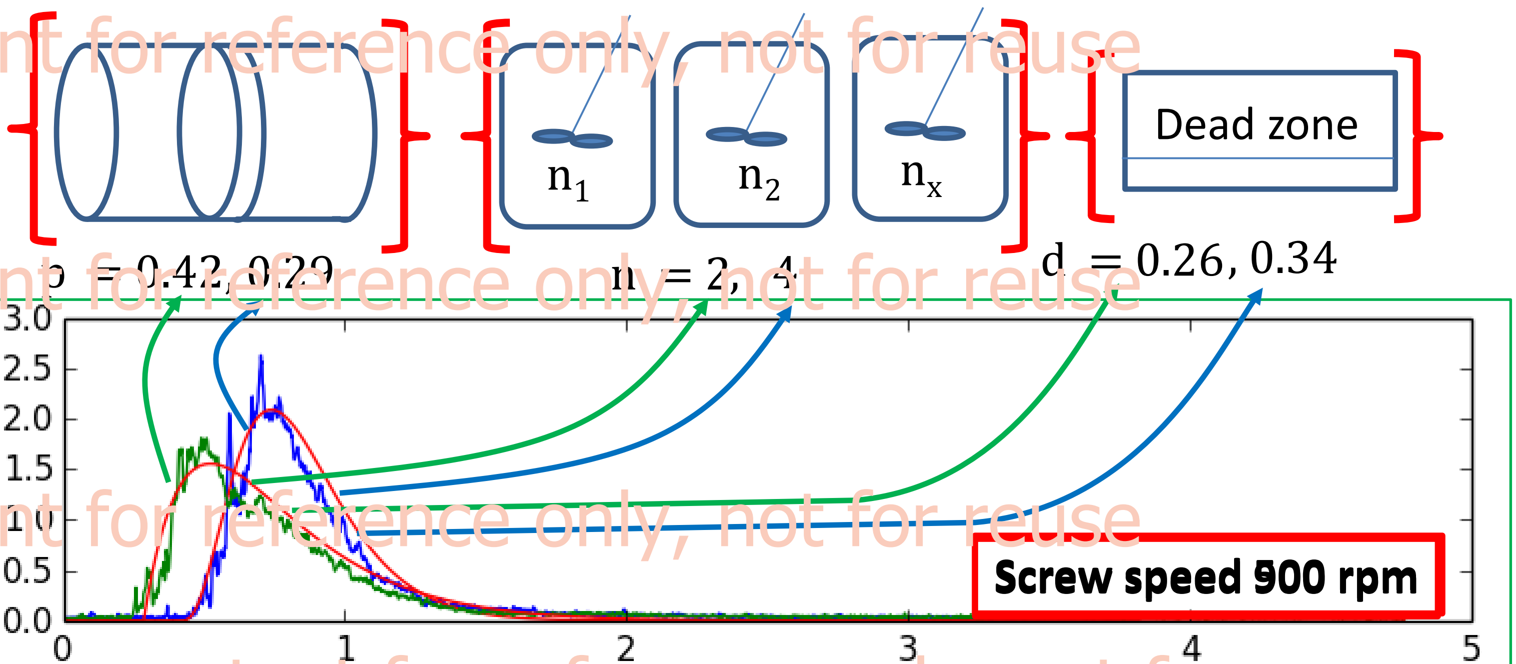
Measurement based
- Mean residence time
- Mean centred variance

Model based
- Number of CSTR
- Plug flow fraction
- Dead volume fraction

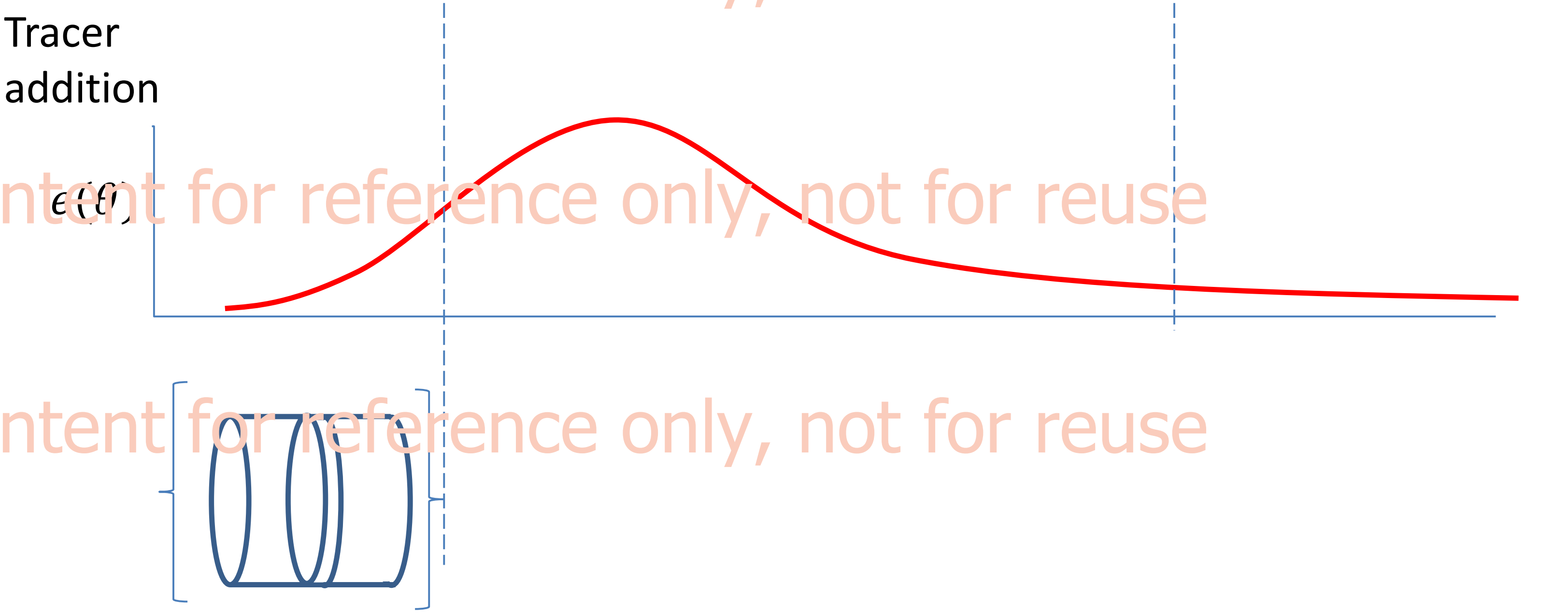
Parameters of the TIS model estimated using experimental RTD based on least SSE

$$e(\theta) = \frac{b[b(\theta - p)]^{n-1}}{(n-1)!} e^{[-b(\theta - p)]}$$

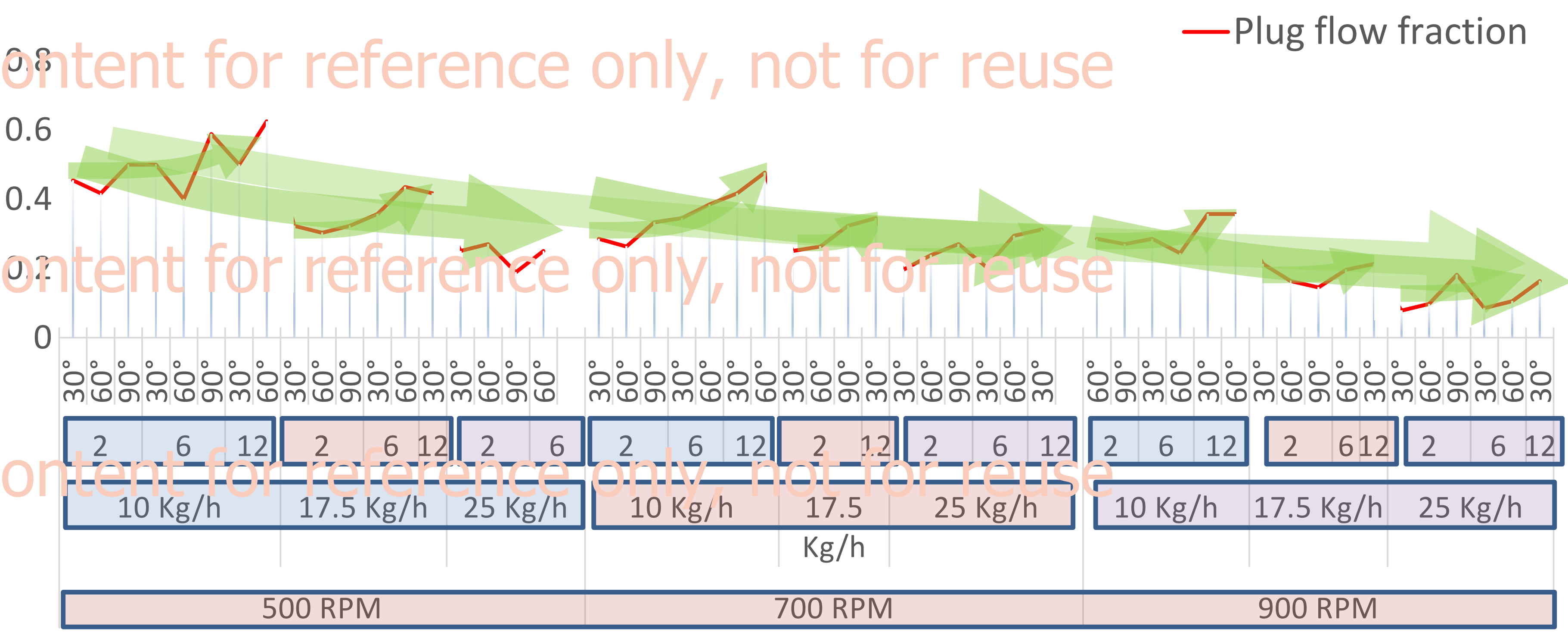
where, $$b = \frac{n}{(1-p)(1-d)}$$



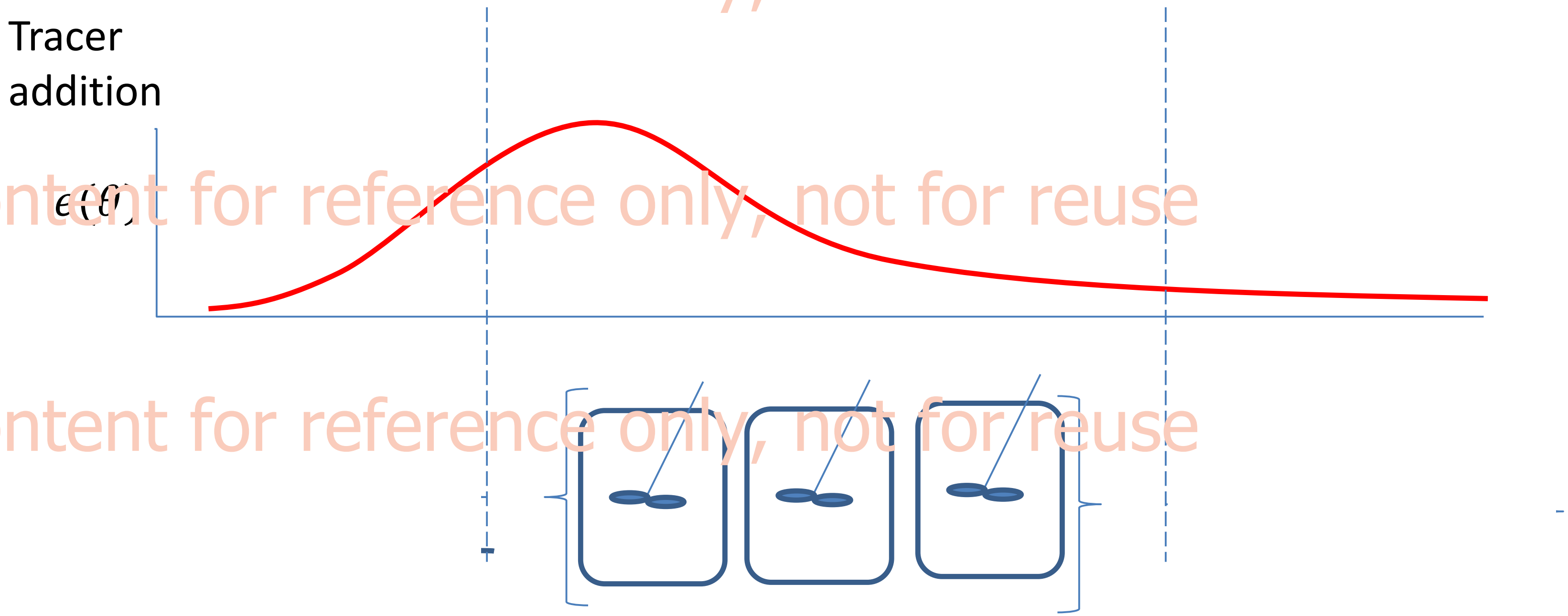
Plug flow component of the RTD



Plug flow fraction decreases with increase in screw speed and throughput



Mixed flow component of the RTD



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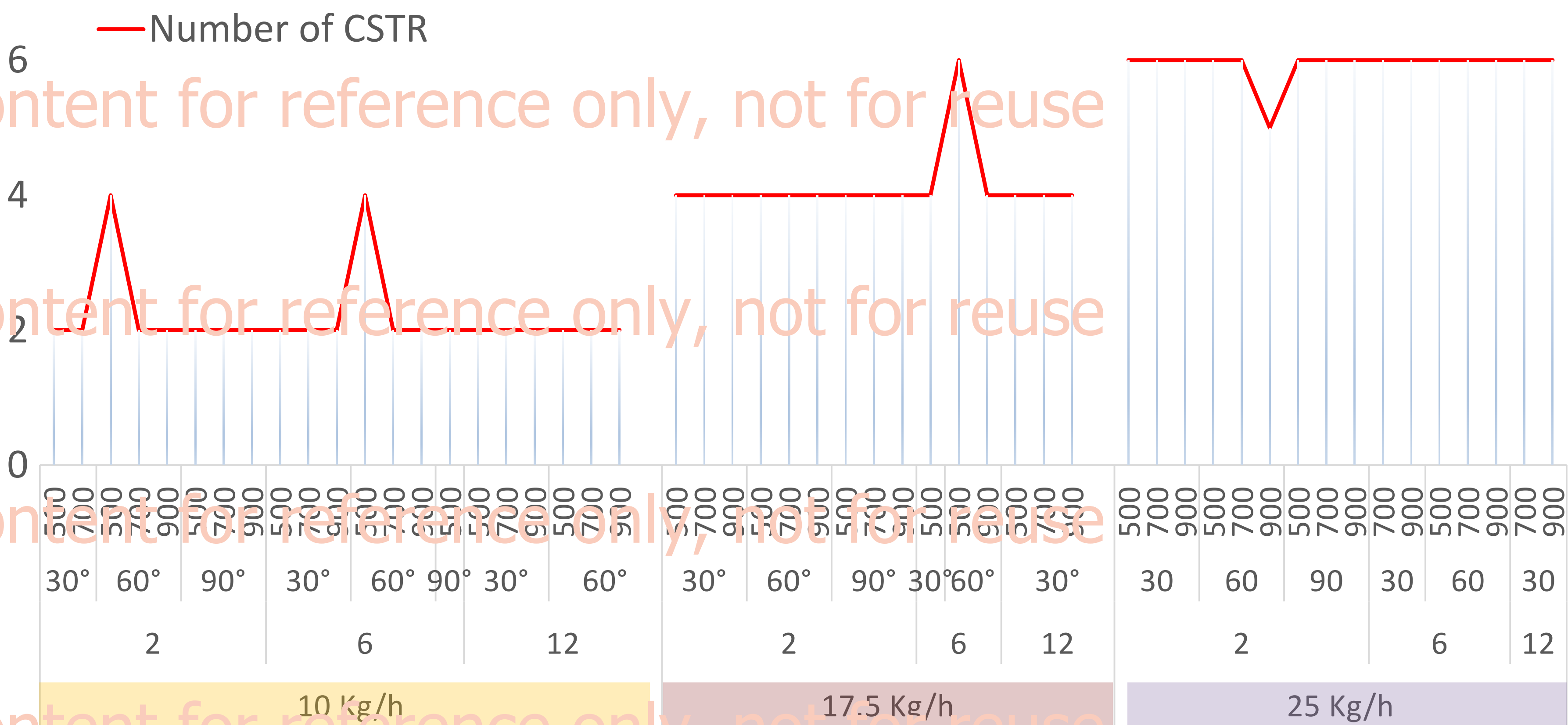
Material throughput controls mixing which reduces with increase in throughput



Mixed flow component of the RTD

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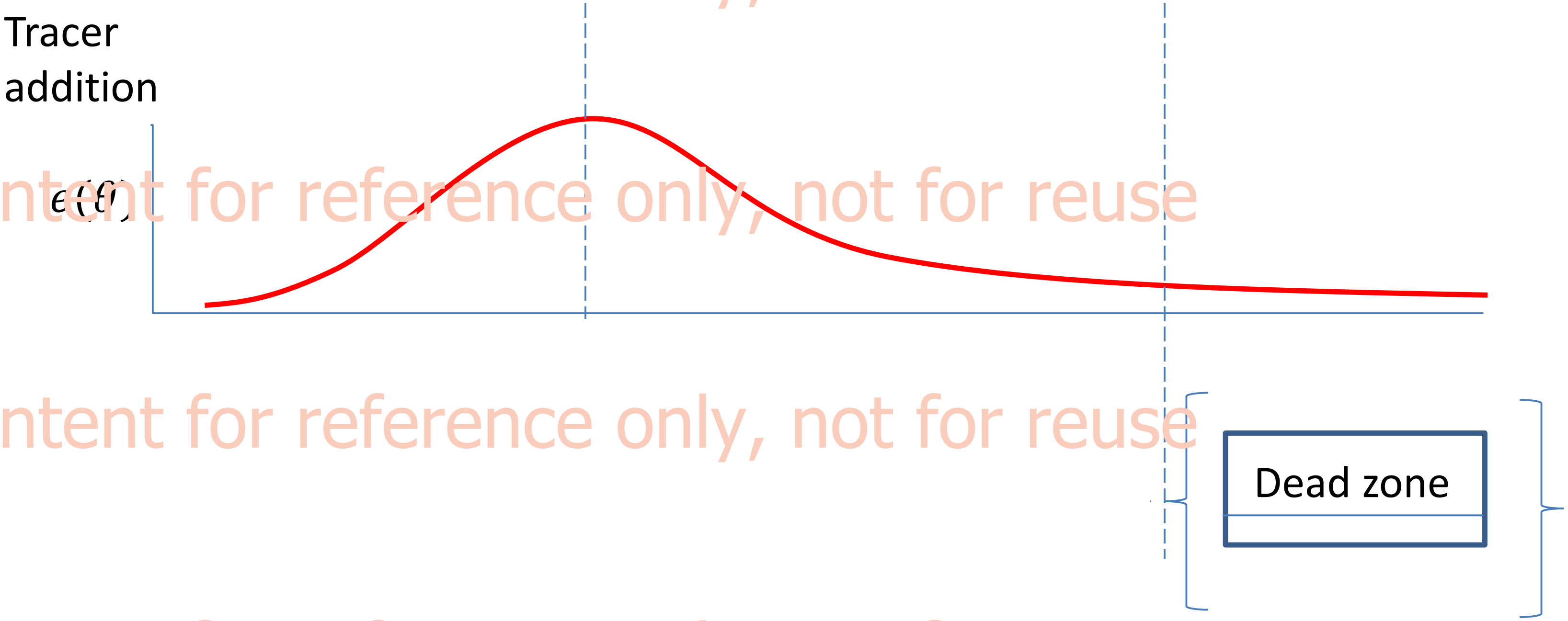

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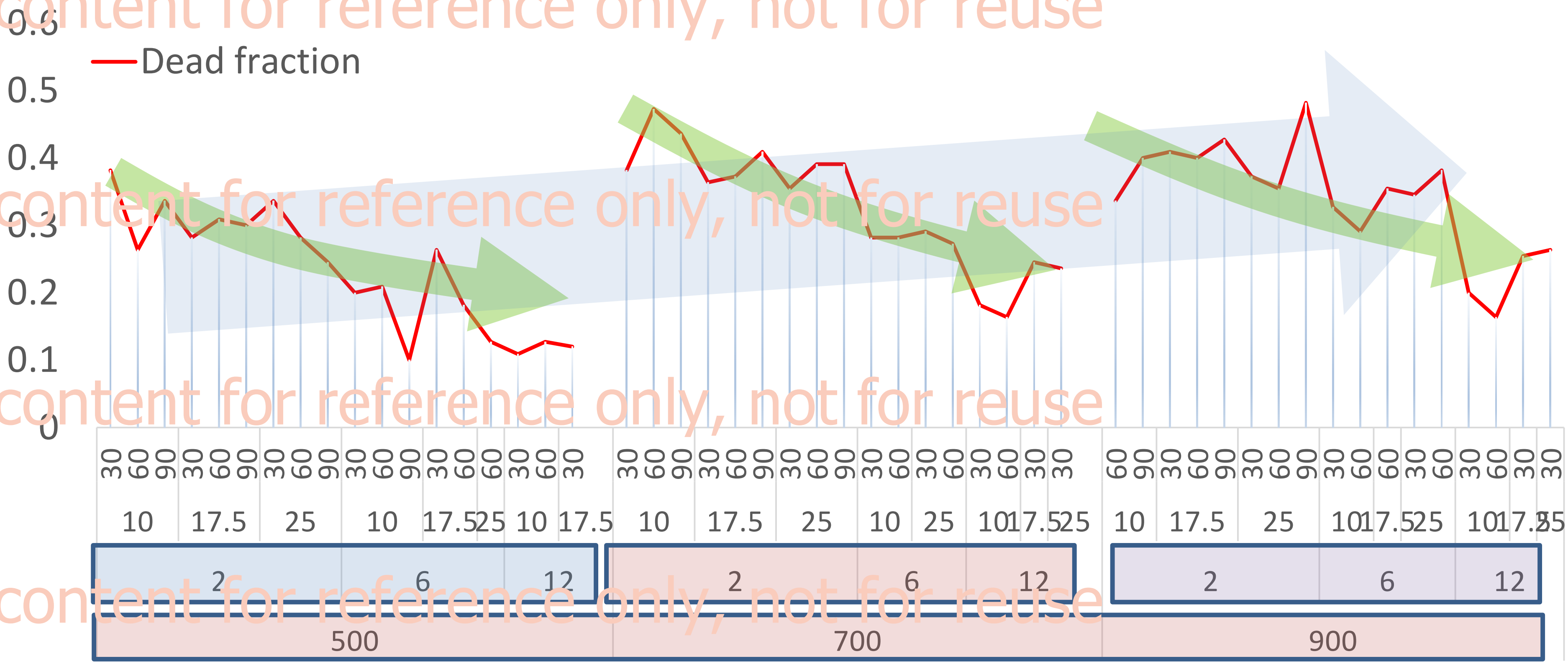
Dead zone increases with screw speed, and reduces with increase in kneading discs



Model based analysis showed that

Screw speed reduces the conveying fraction

Material throughput dictates mixing.

Number of kneading discs help to reduce the dead volume in TSG

Conclusions

NIR-based chemical imaging is fast and robust technique for RTD studies.

Along with experimental study, an improved insight by model based analysis of RTD.

Screw speed controls the residence time, while the material throughput controls mixing.

Perspectives

Together with a Granule size distribution study it will be confirmed which mixing regime is most desirable.

In further study we will investigate material properties influence on the RTD and mixing.

Utilise the mixing and residence time information for mechanistic modeling of the TSG.

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