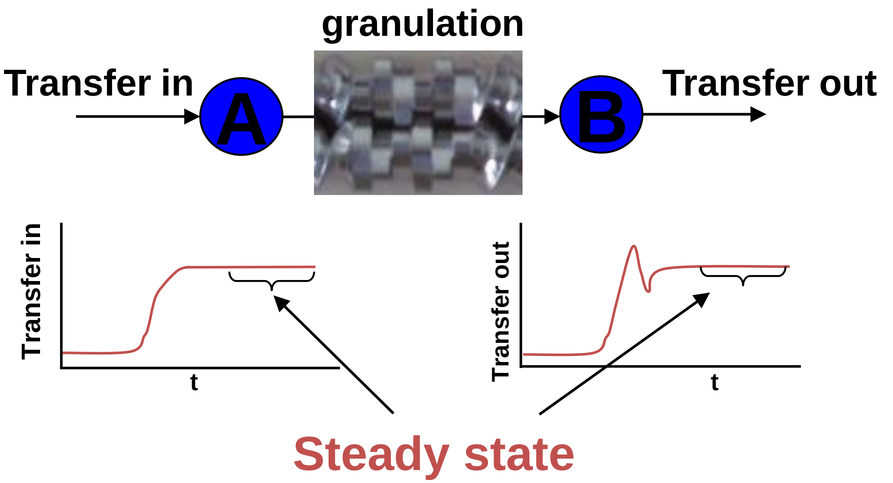
GEA Event

Ashish Kumar

At appropriate time-scales and conditions, granulation is in steady state



$$transfer\ in \approx \text{constant} \approx transfer\ out$$

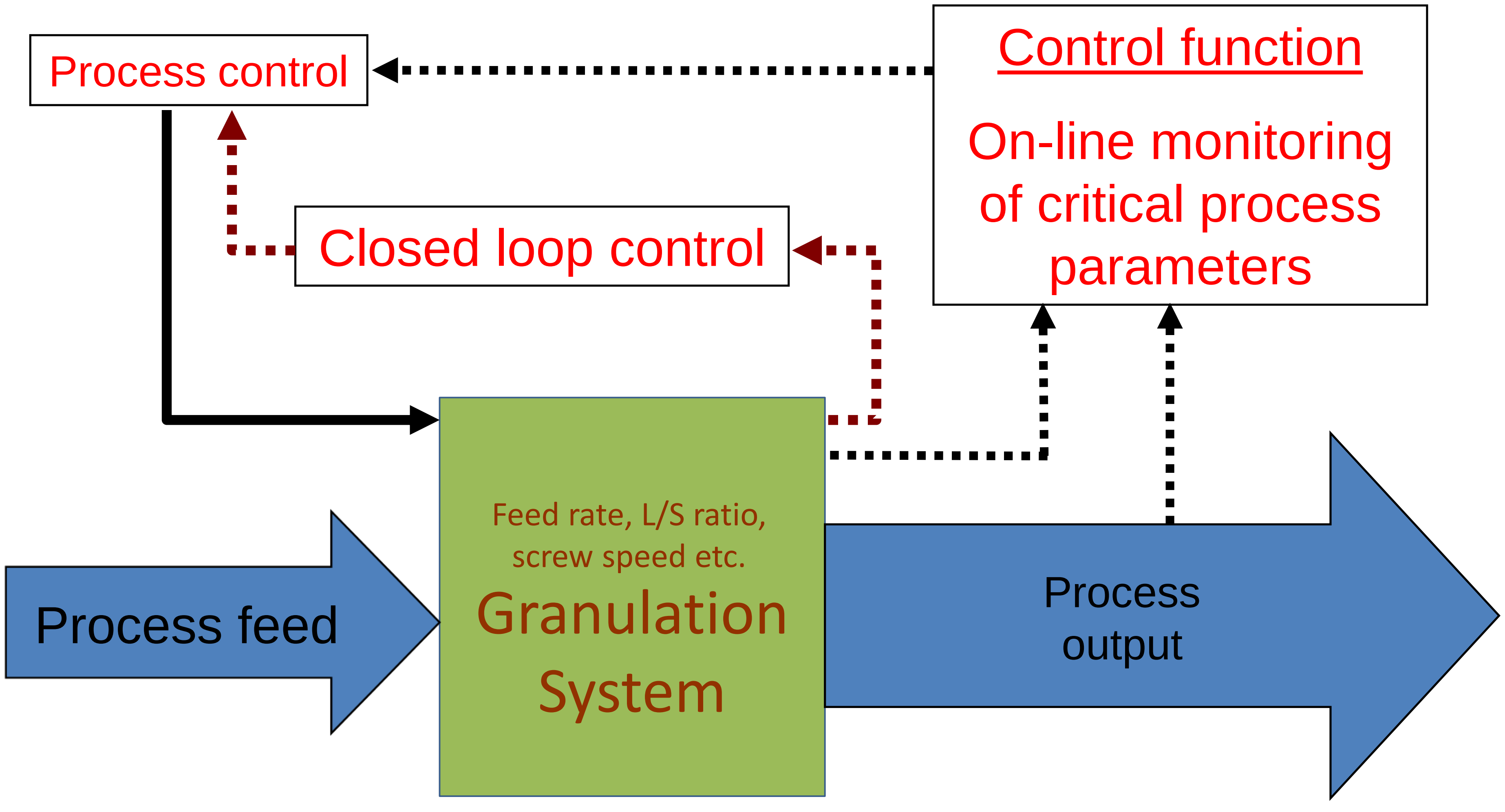
$$\frac{d[P_m]}{dt} \approx 0 \approx \frac{d[G_m]}{dt}$$

Two key implications

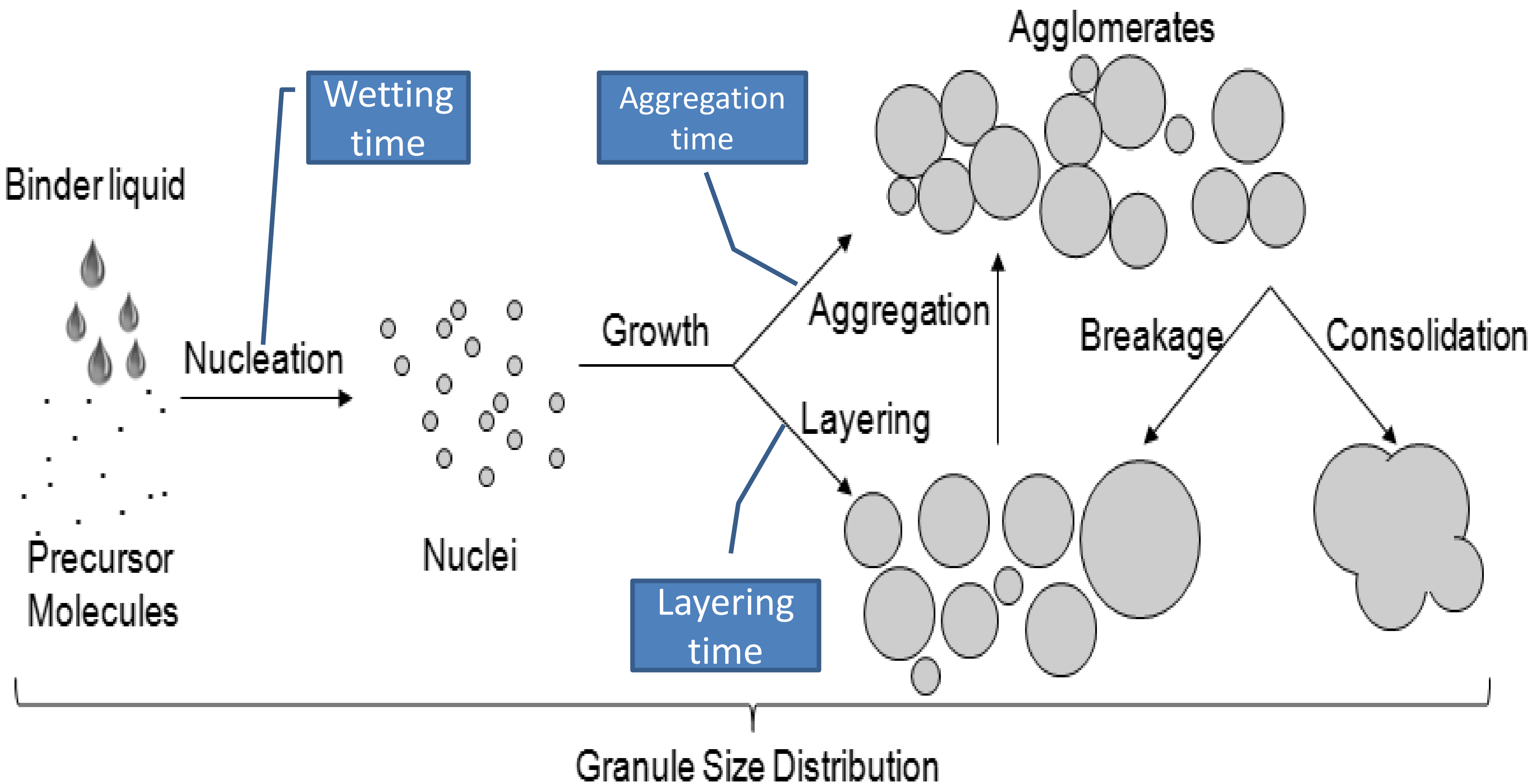
1. Fluxes are roughly constant (Dynamics are transient)

2. If feed is constant, product quality is consistent!

Scope: Desired Outcome



Twin-Screw Granulator applies High Shear Wet Granulation

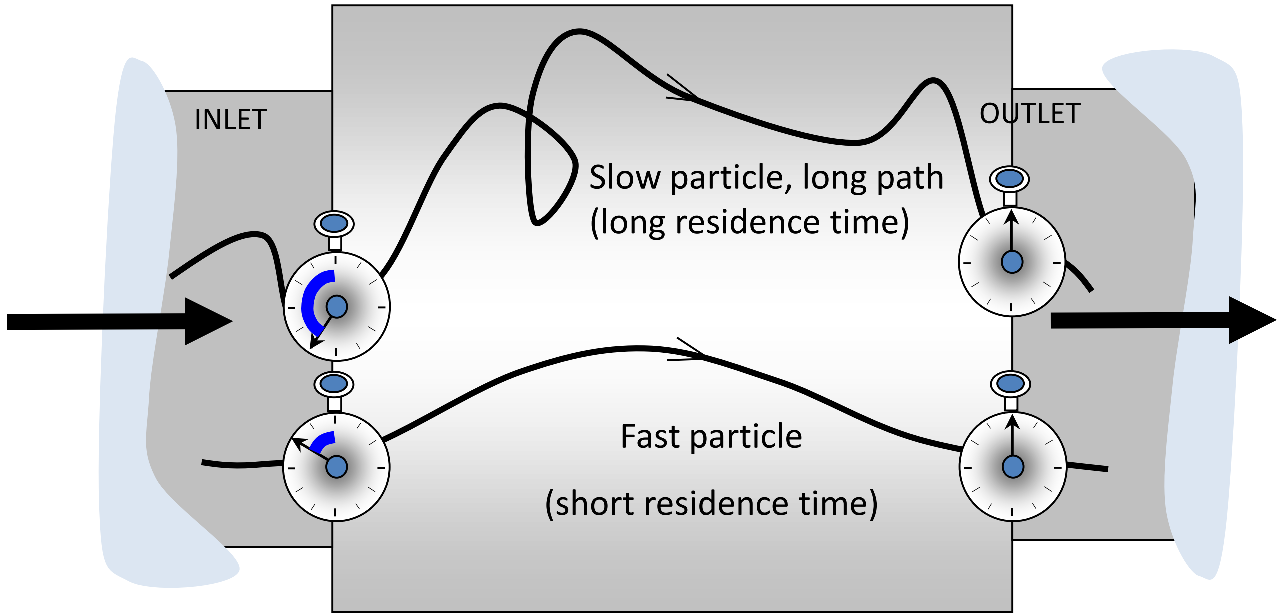


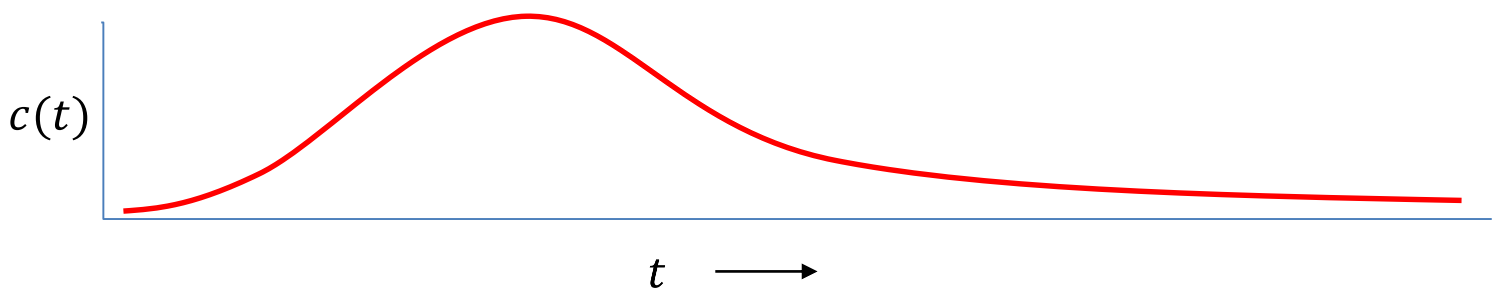
Key questions for twin-screw granulation process development

What affects granulation time and mixing?

What control degree of rate processes involved in desired quality of granules?

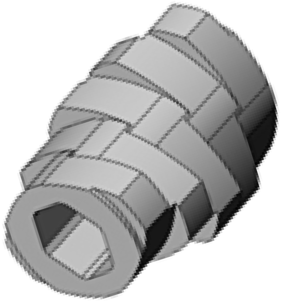
Residence time distribution to know the granulation time and mixing



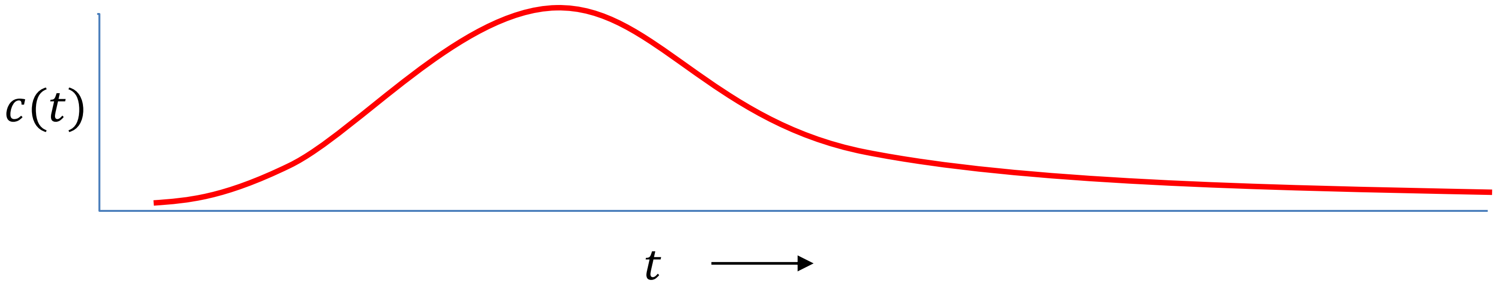


Residence time distribution to know the granulation time and mixing

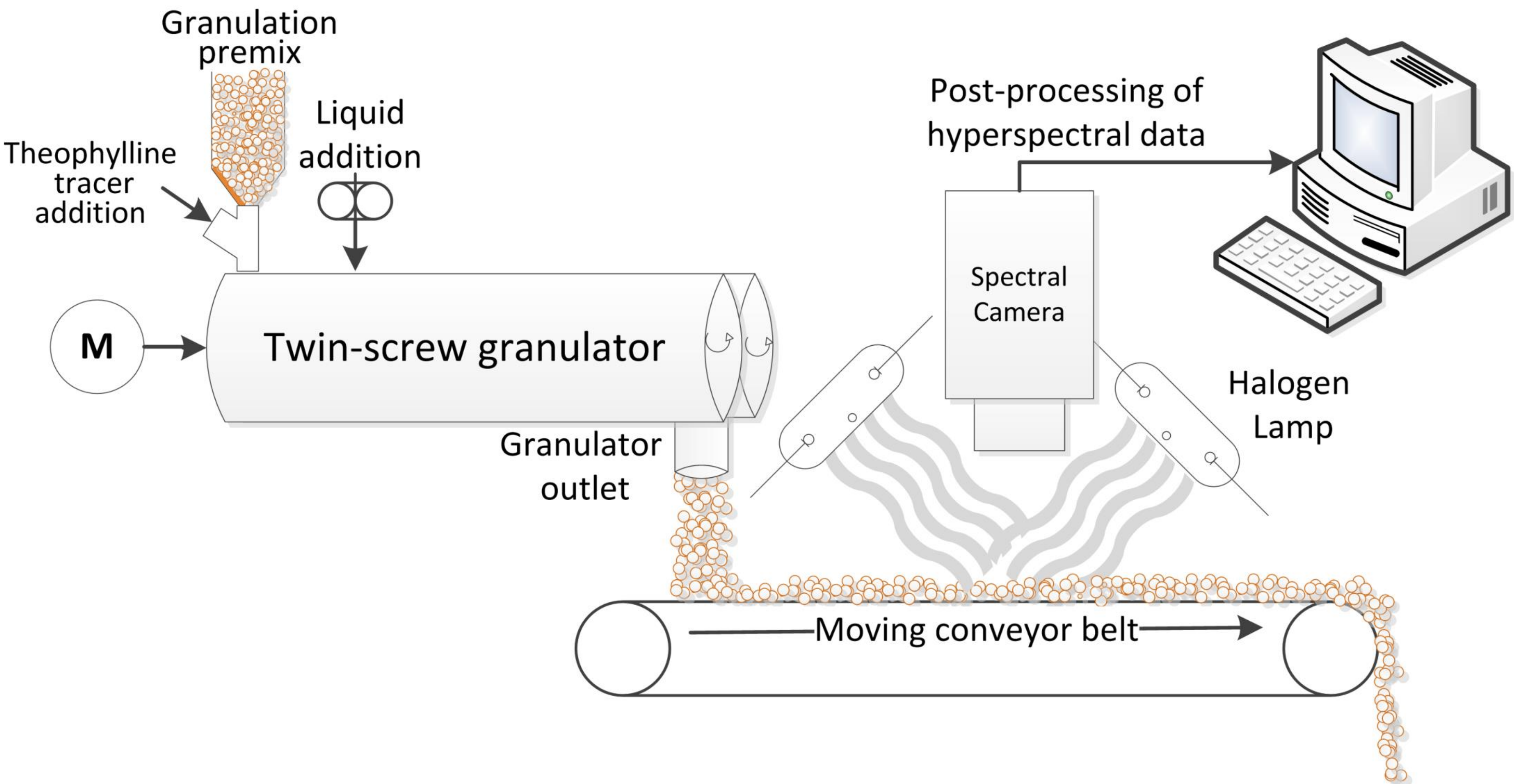
Screw Configuration
- Number of kneading discs
- Stagger angle



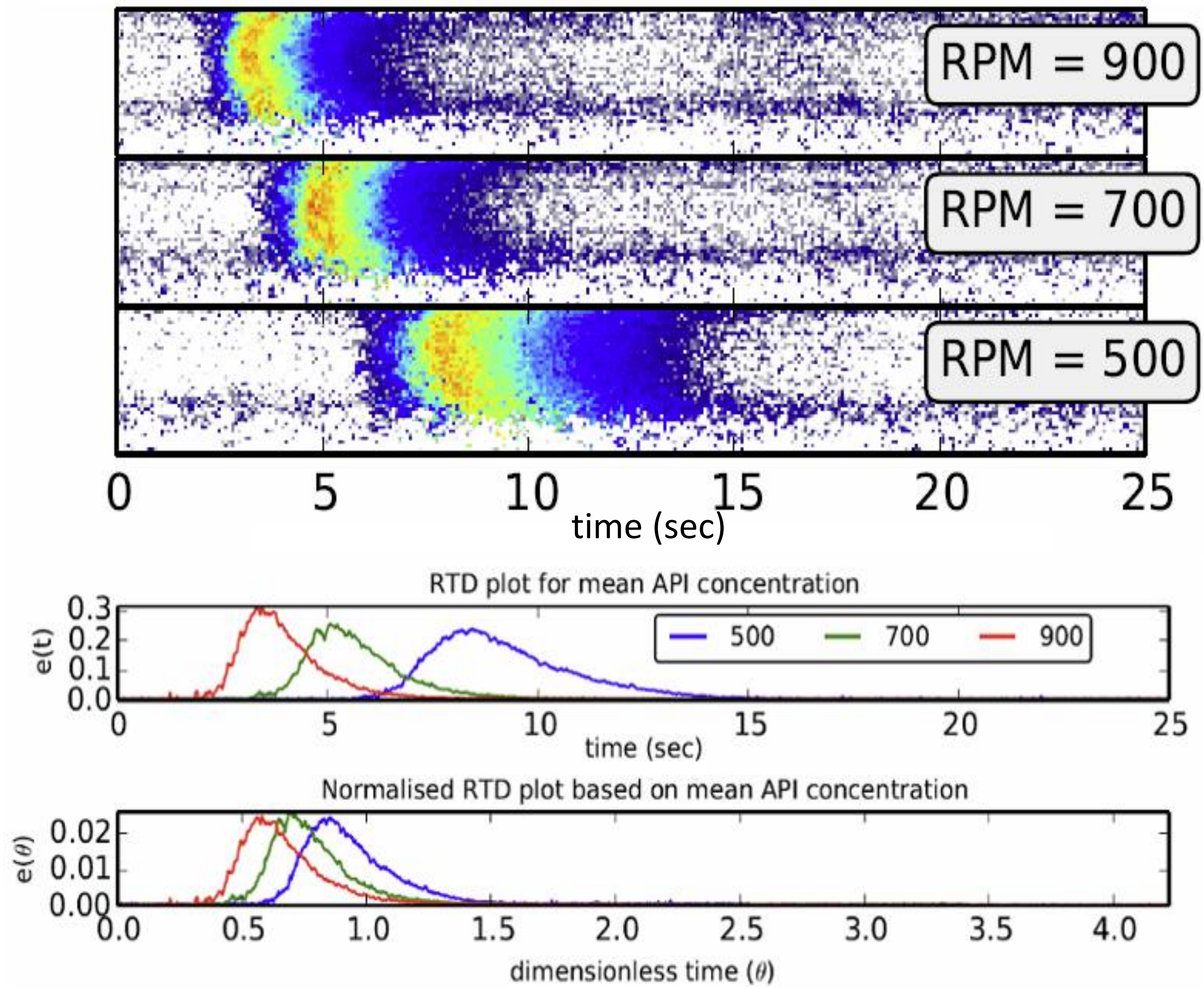
Process parameters
- Material throughput
- Screw speed



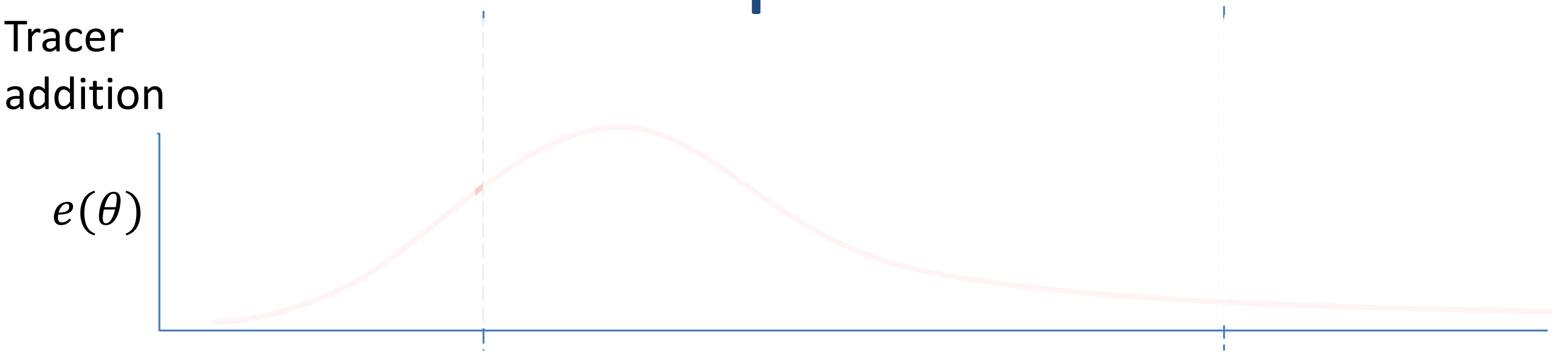
Tracer concentration in granules produced was measured using NIR chemical imaging



API Map was used to measure RTD



Conceptual model to include three main components of RTD

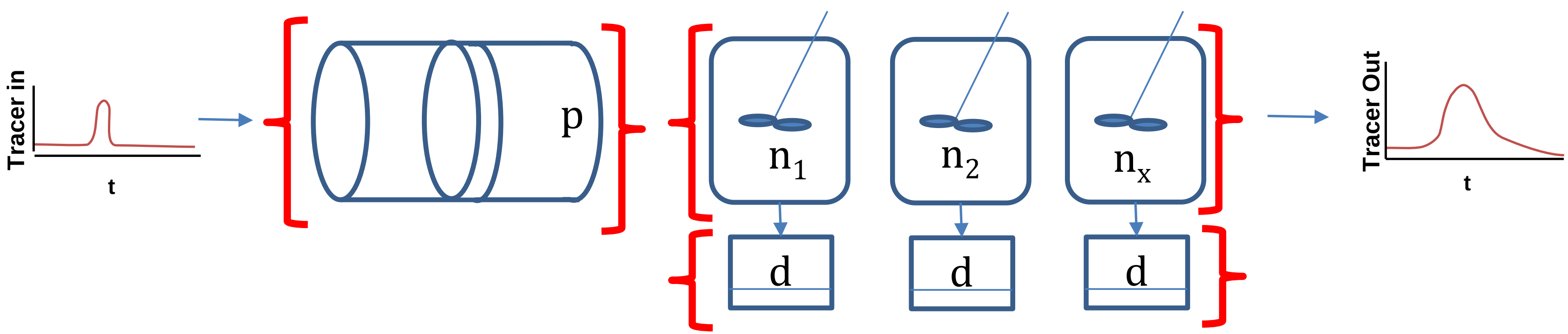


Modified Tank-in-Series model used

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

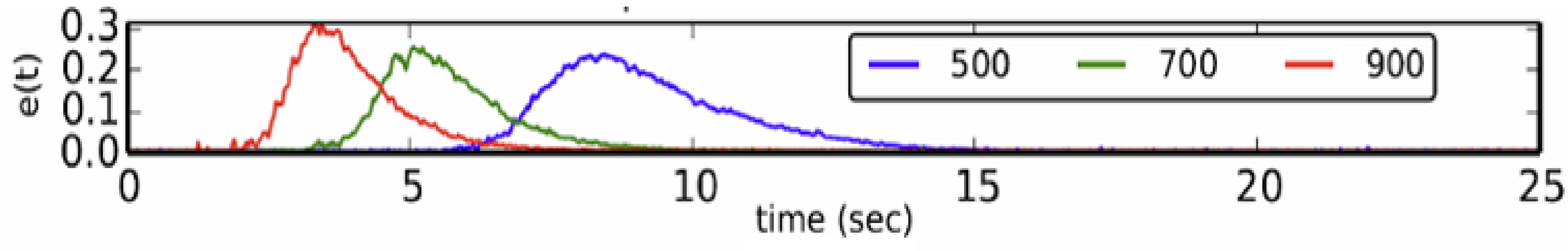
Outcomes

Measurement based

- Mean residence time

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

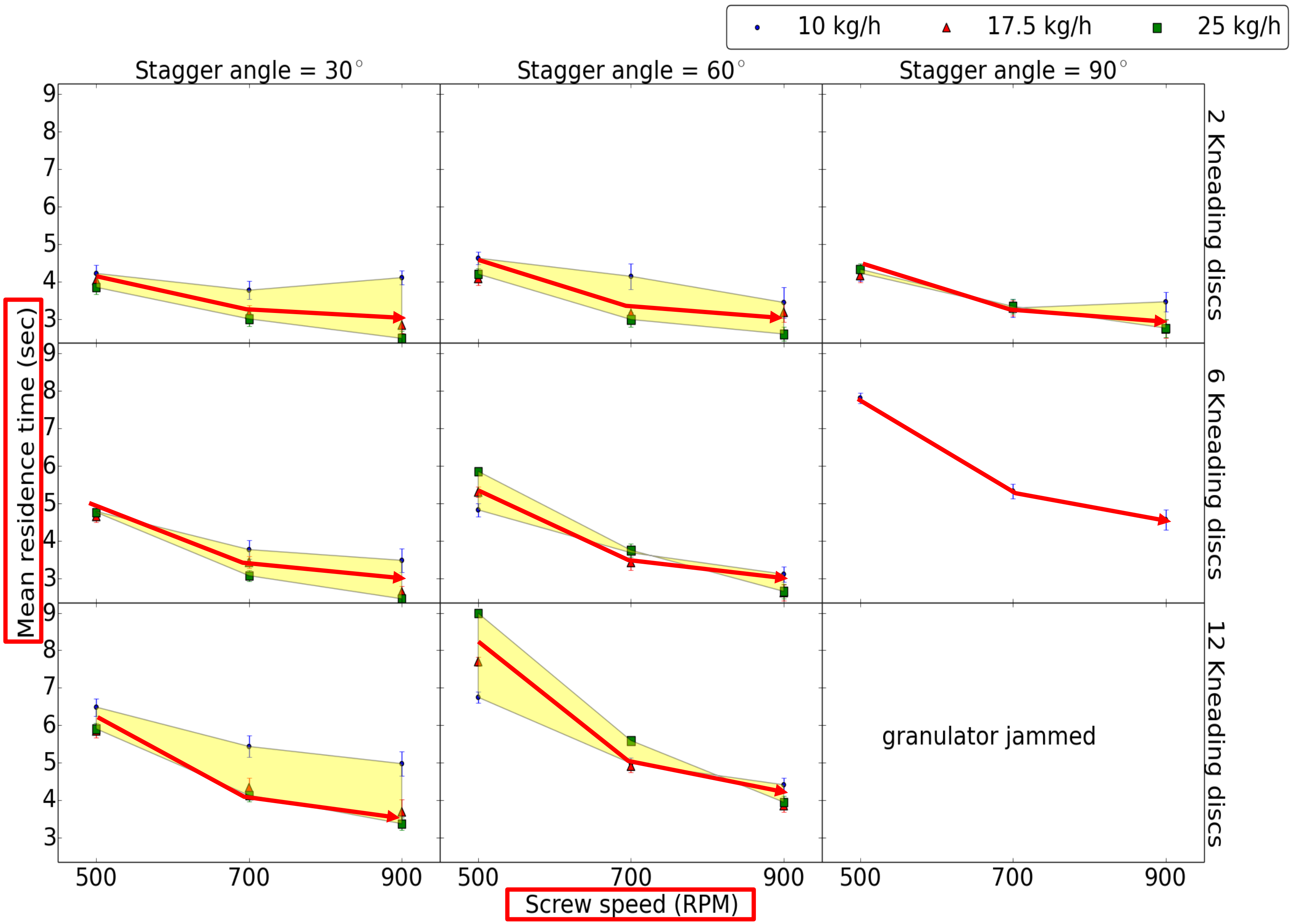
Outcomes

Measurement based
- Mean residence time

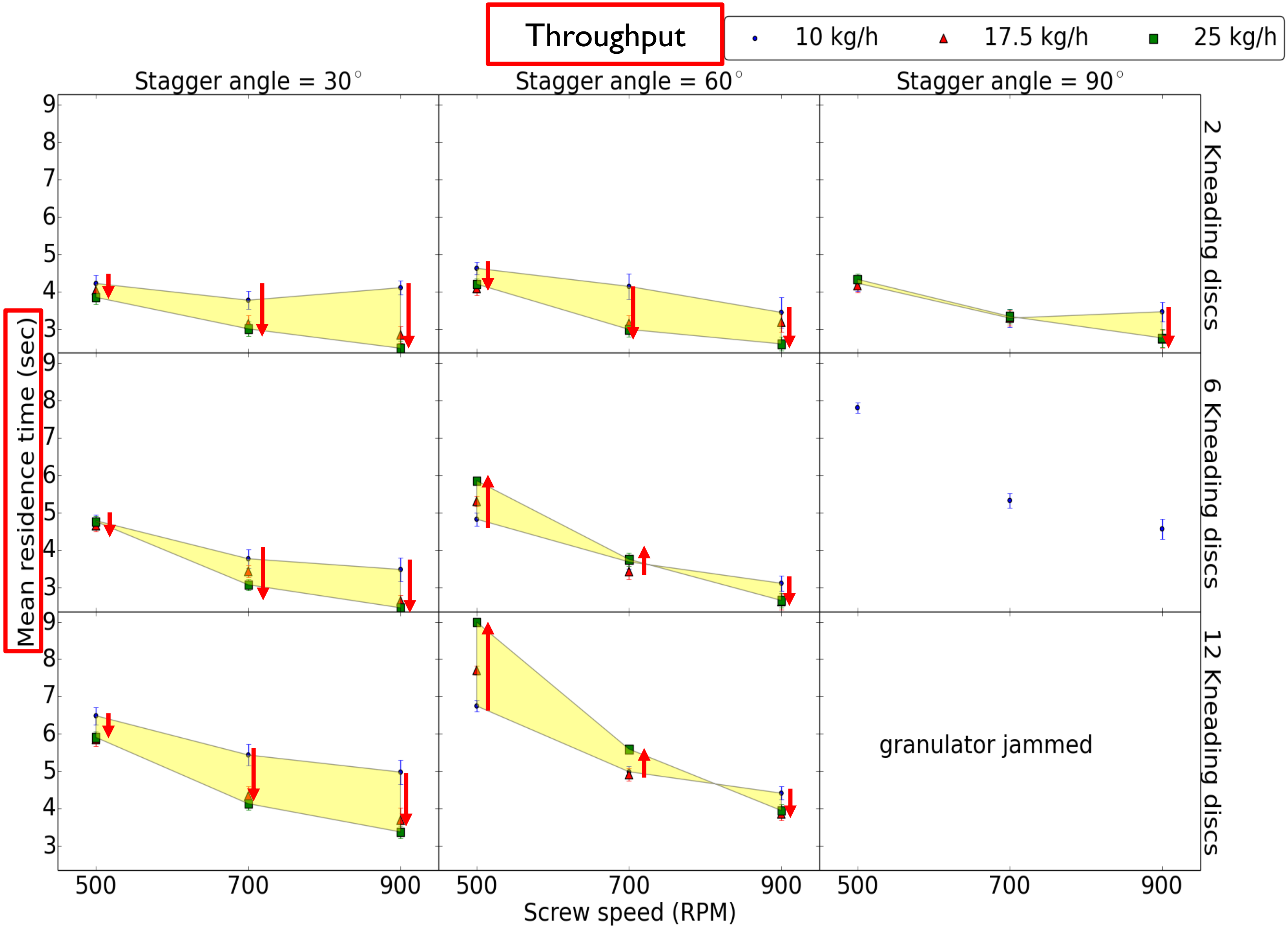
Model based
- Number of CSTR
- Plug flow fraction
- Dead volume fraction

Residence time reduces with increase in screw speed

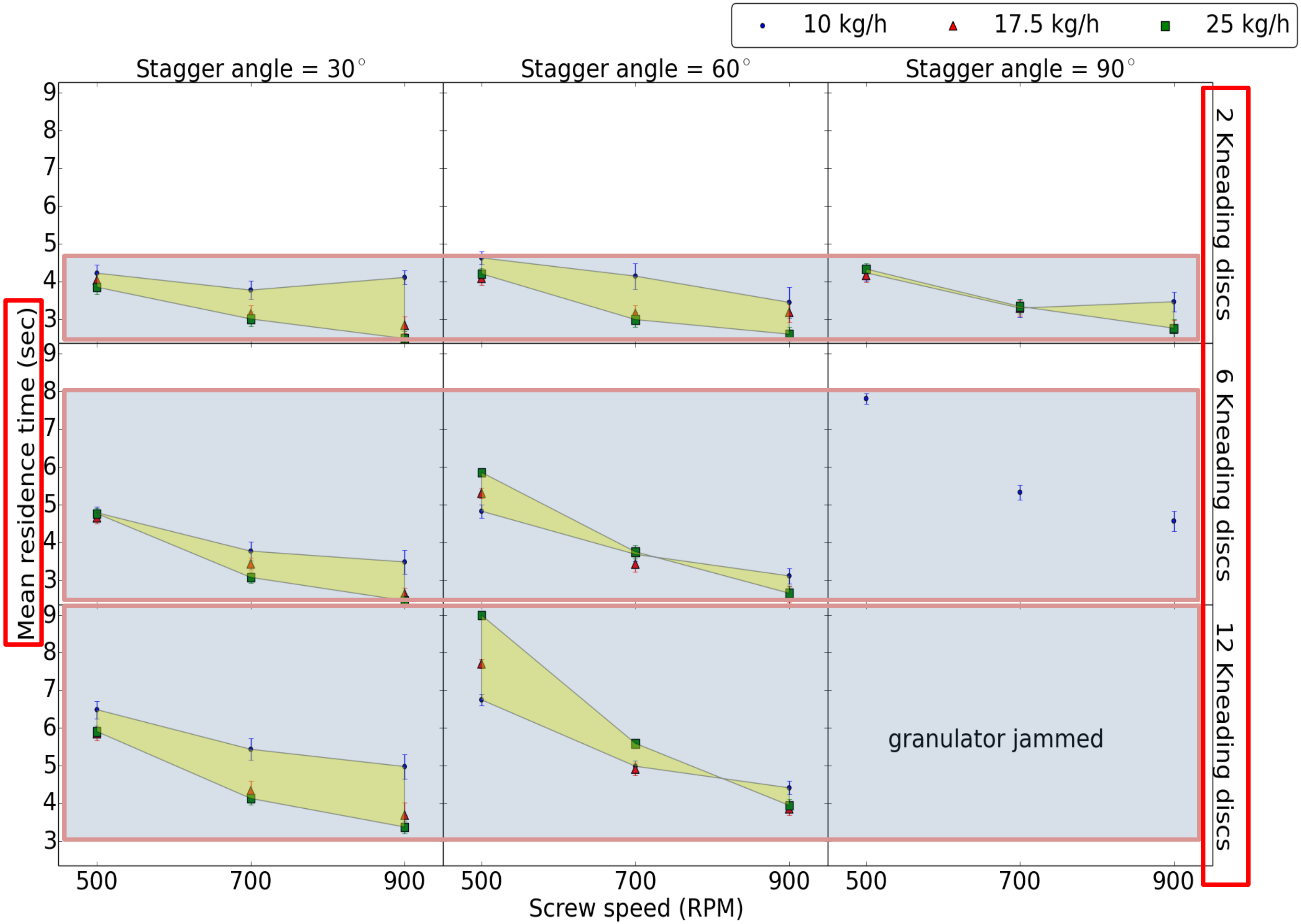
Measure of the mean of the distribution



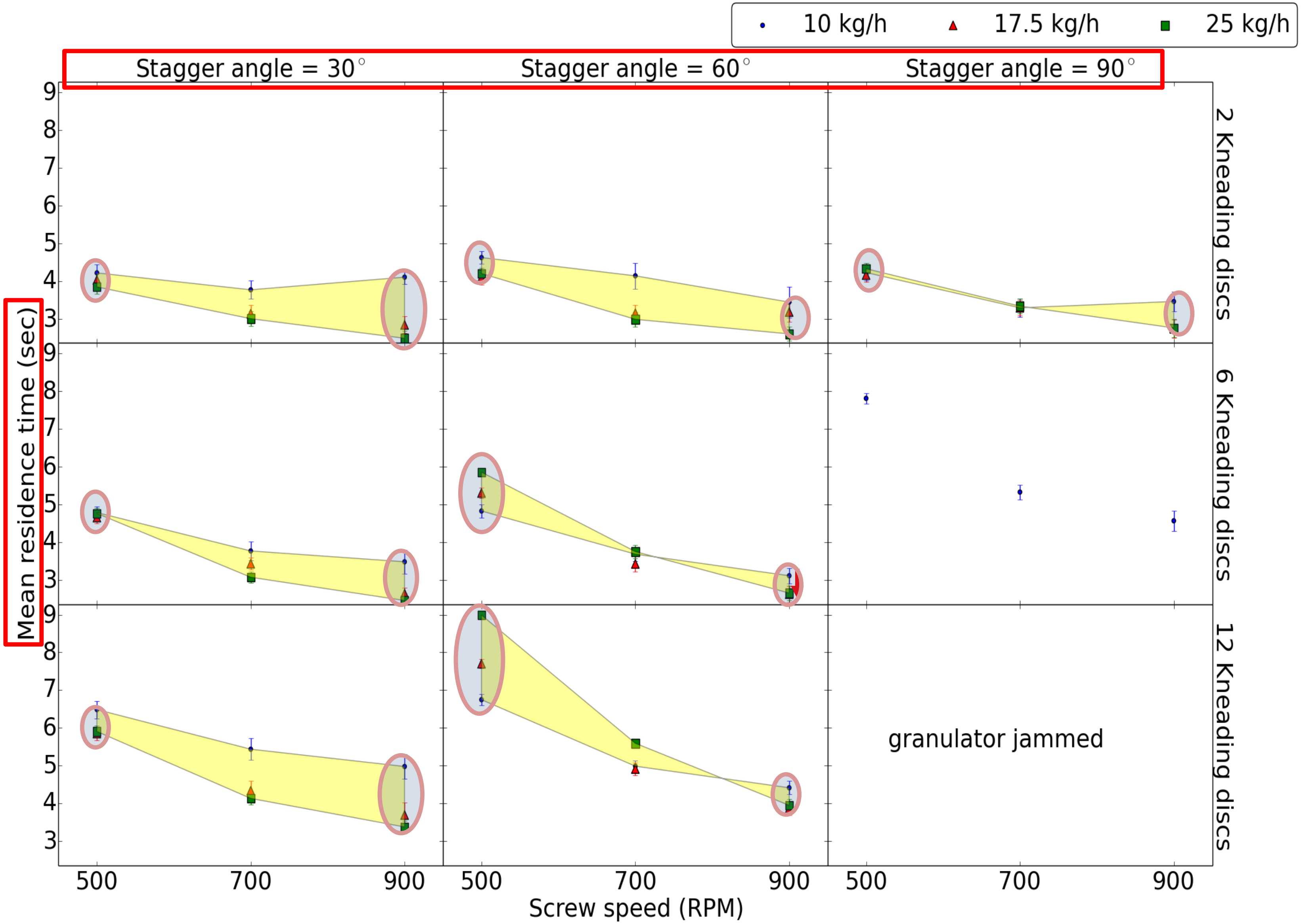
Residence time reduces with increase in throughput…but not always



Residence time increases with increase in number of kneading discs.



Residence time reduces with increase in stagger angle.



Mean of the residence time distribution

Number of kneading discs

Throughput & stagger angle

Screw Speed

Analysis of residence time distribution in twin-screw granulation

Chemical imaging based RTD measurement

Model Formulation

Outcomes

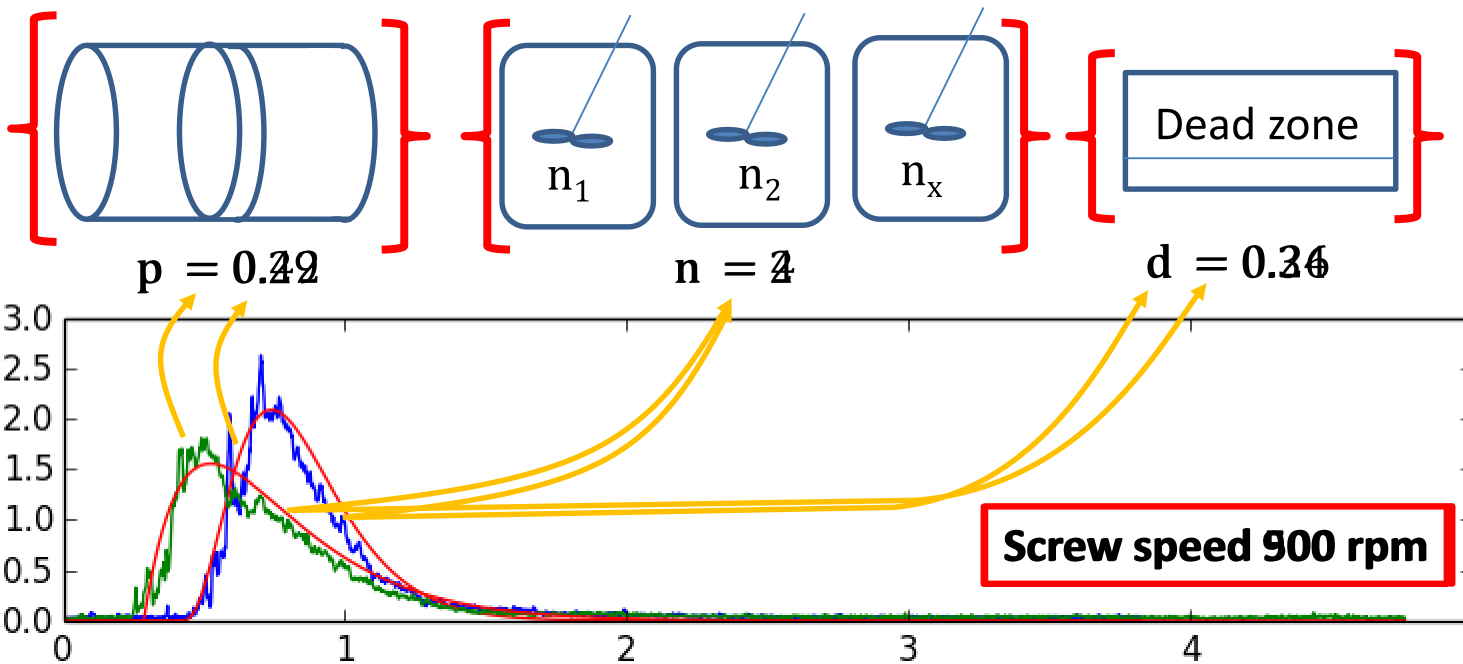
Measurement based
- Mean residence time
- Mean centred variance

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

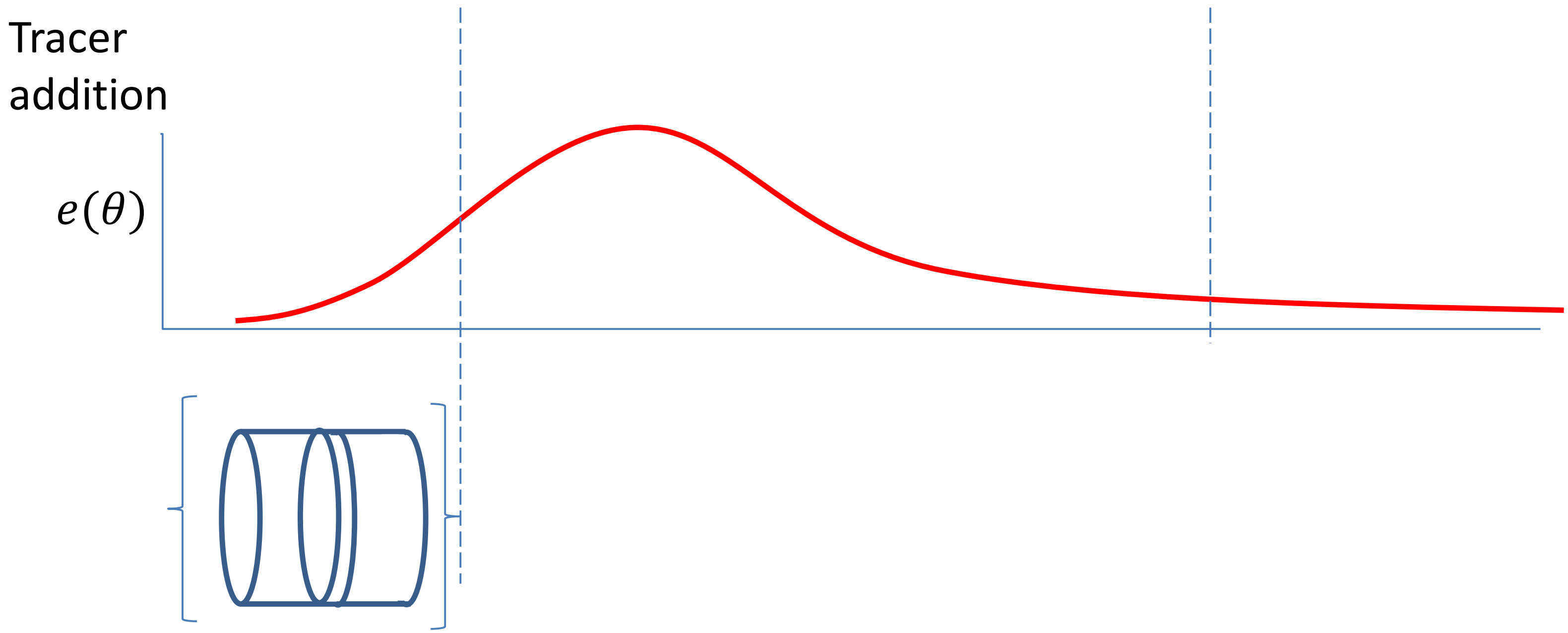
Parameters of the TIS model estimated using experimental RTD based on least SSE

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

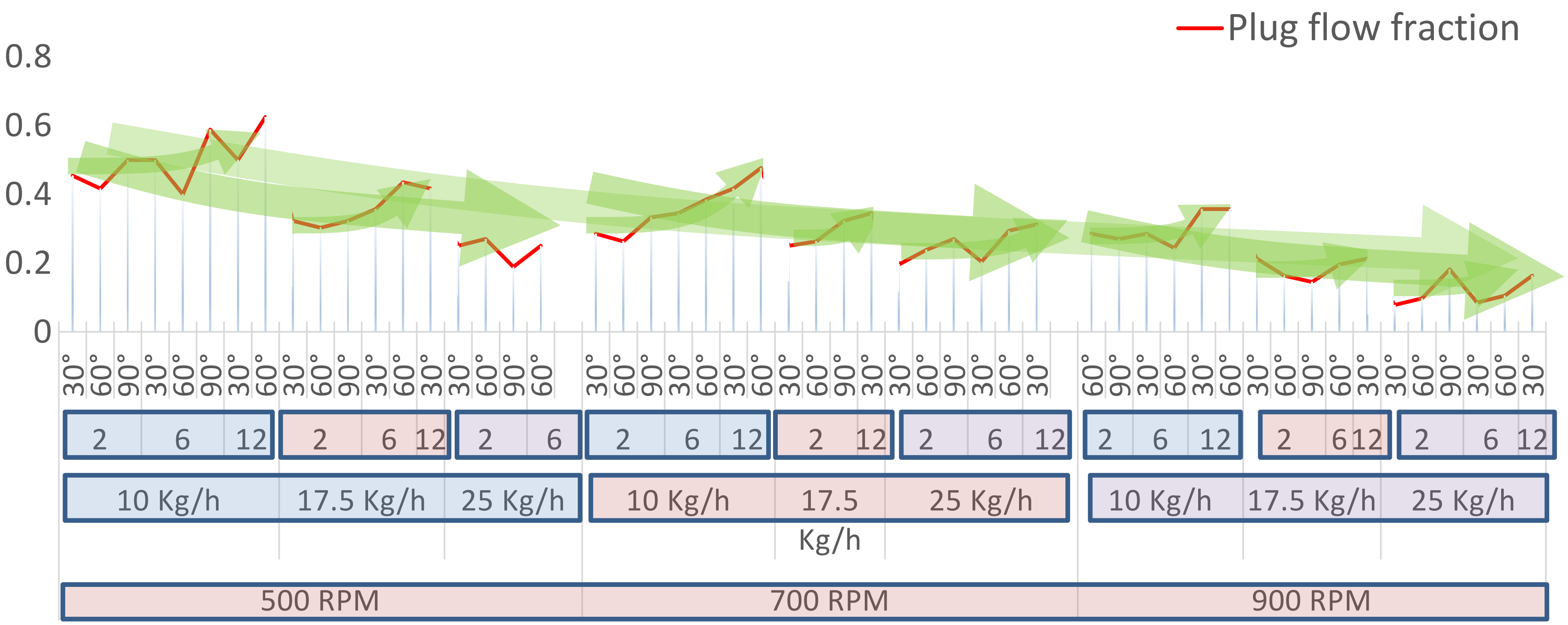
where, $b = \frac{n}{(1-p)(1-d)}$



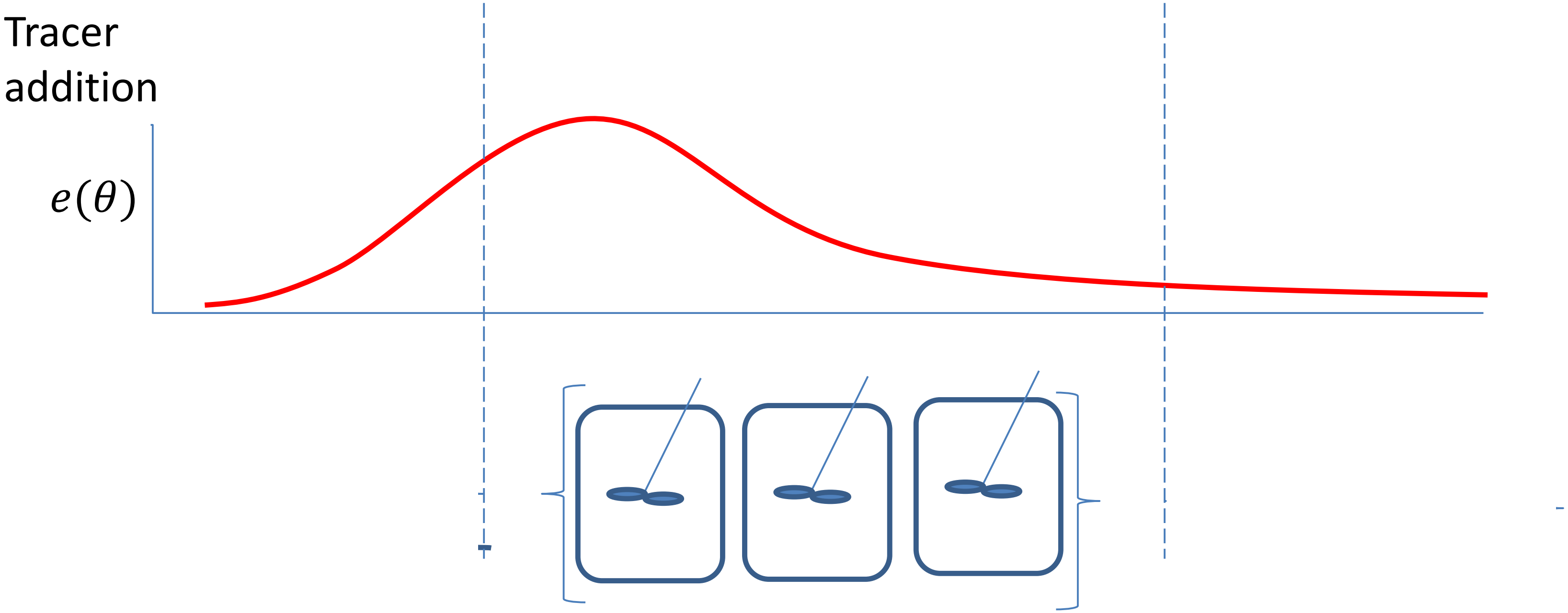
Plug flow component of the RTD



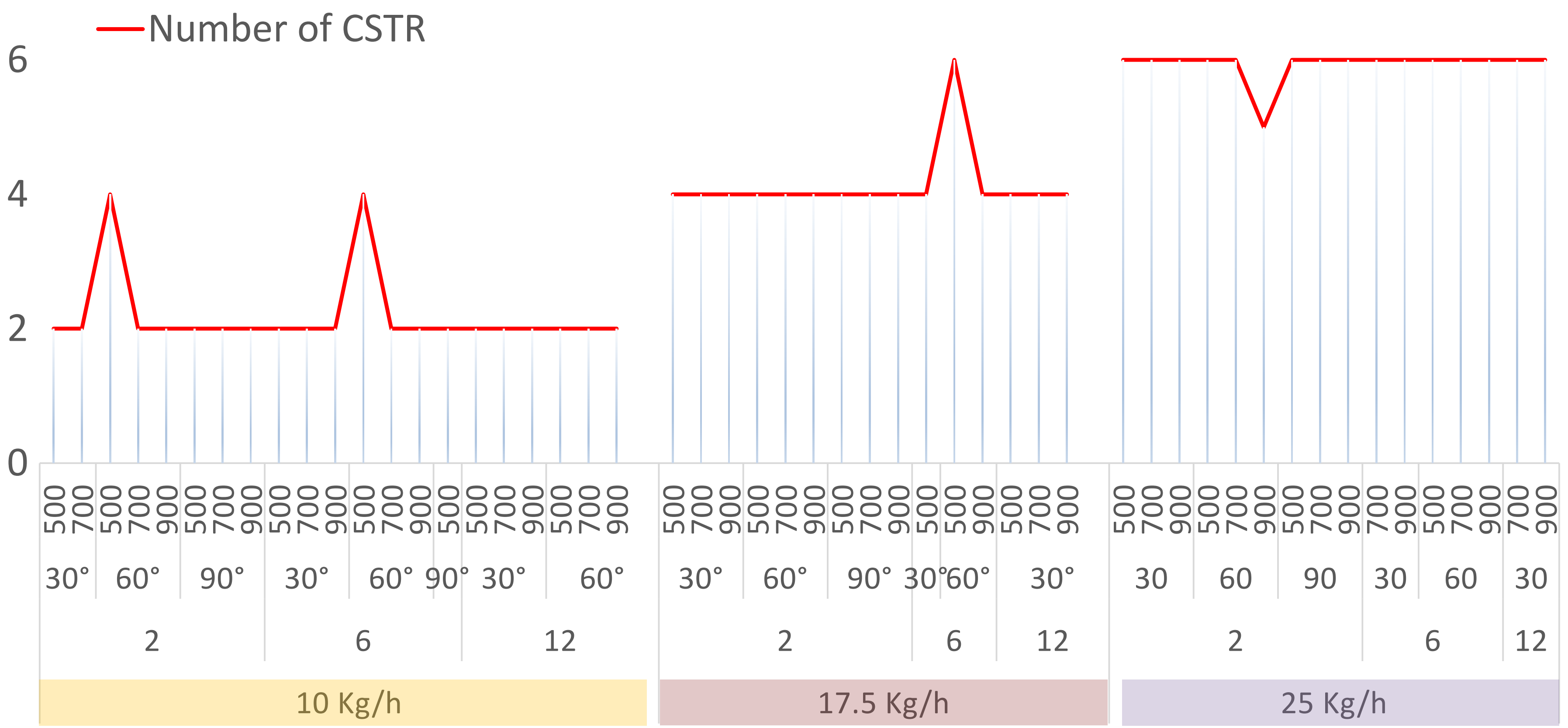
Plug flow fraction decreases with increase in screw speed and throughput



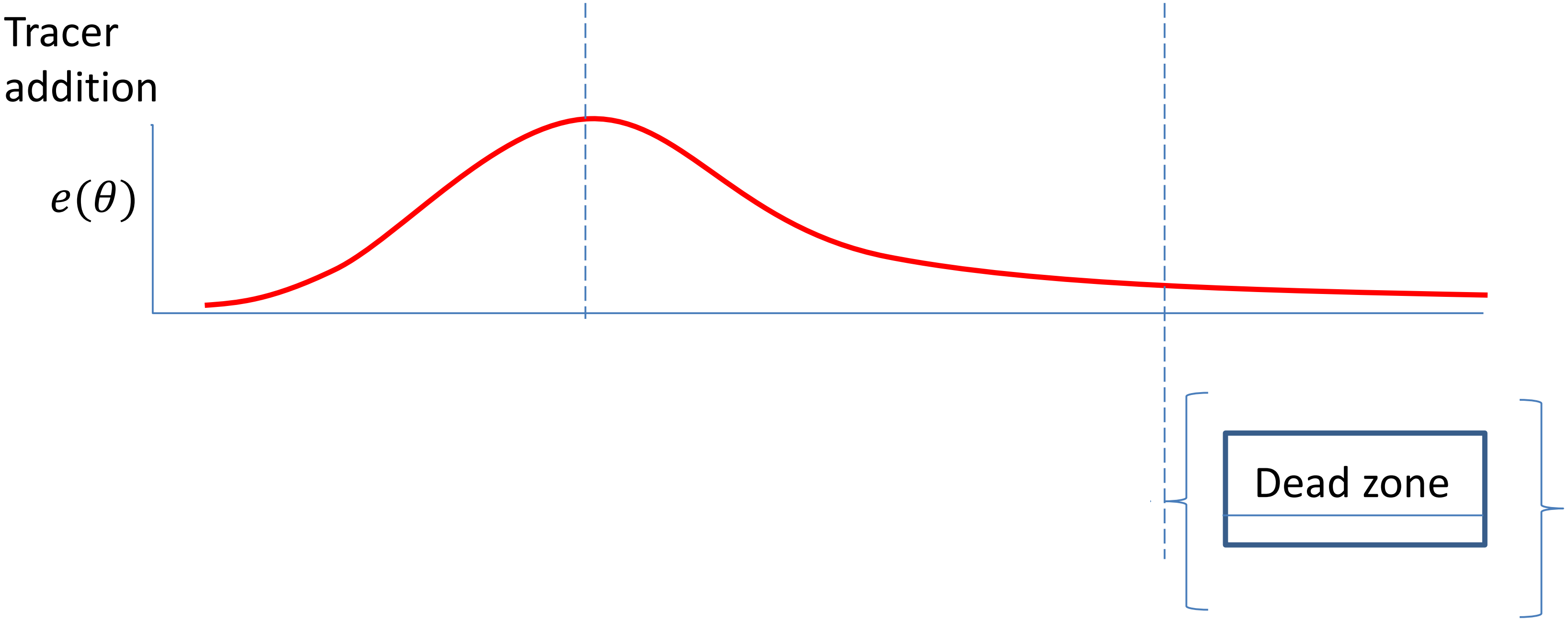
Mixed flow component of the RTD



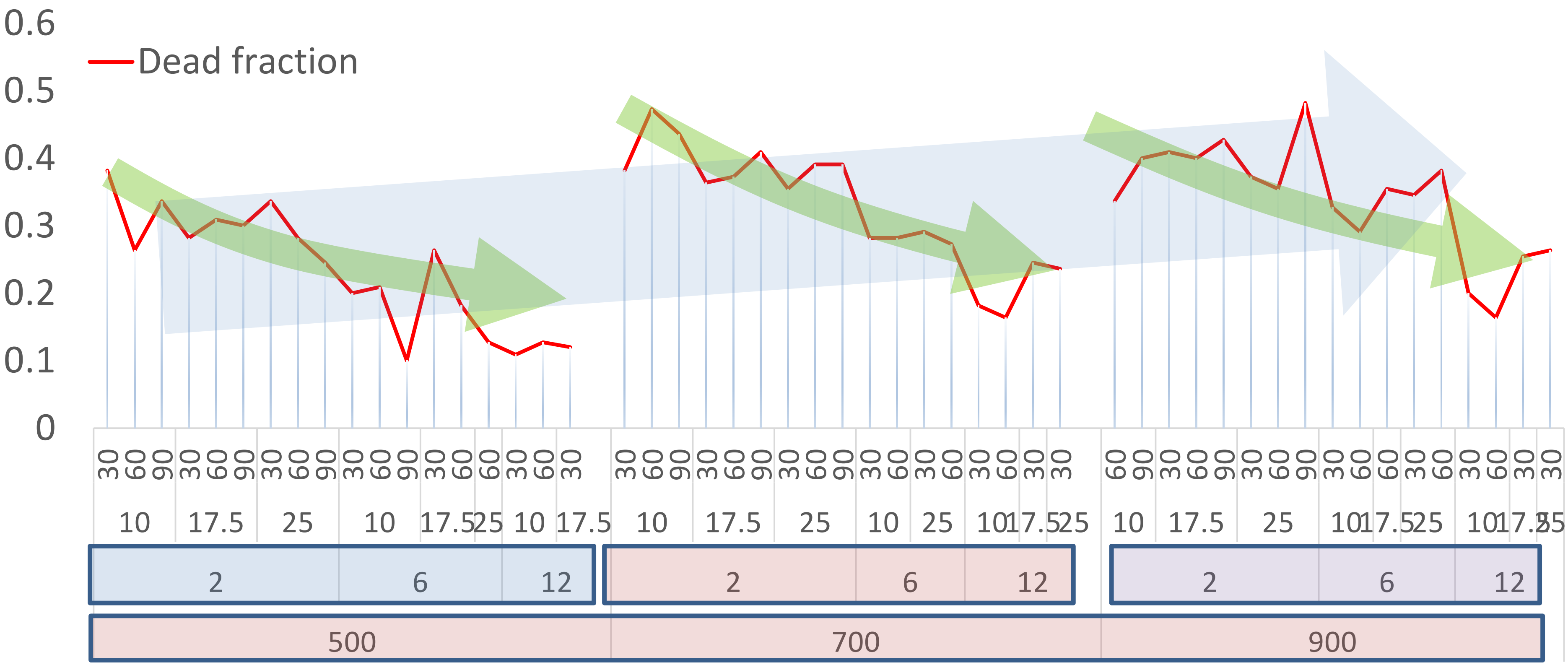
Material throughput controls mixing which reduces with increase in throughput



Mixed flow component of the RTD



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



RTD analysis showed that

Screw speed controls the residence time,

Material throughput controls mixing.

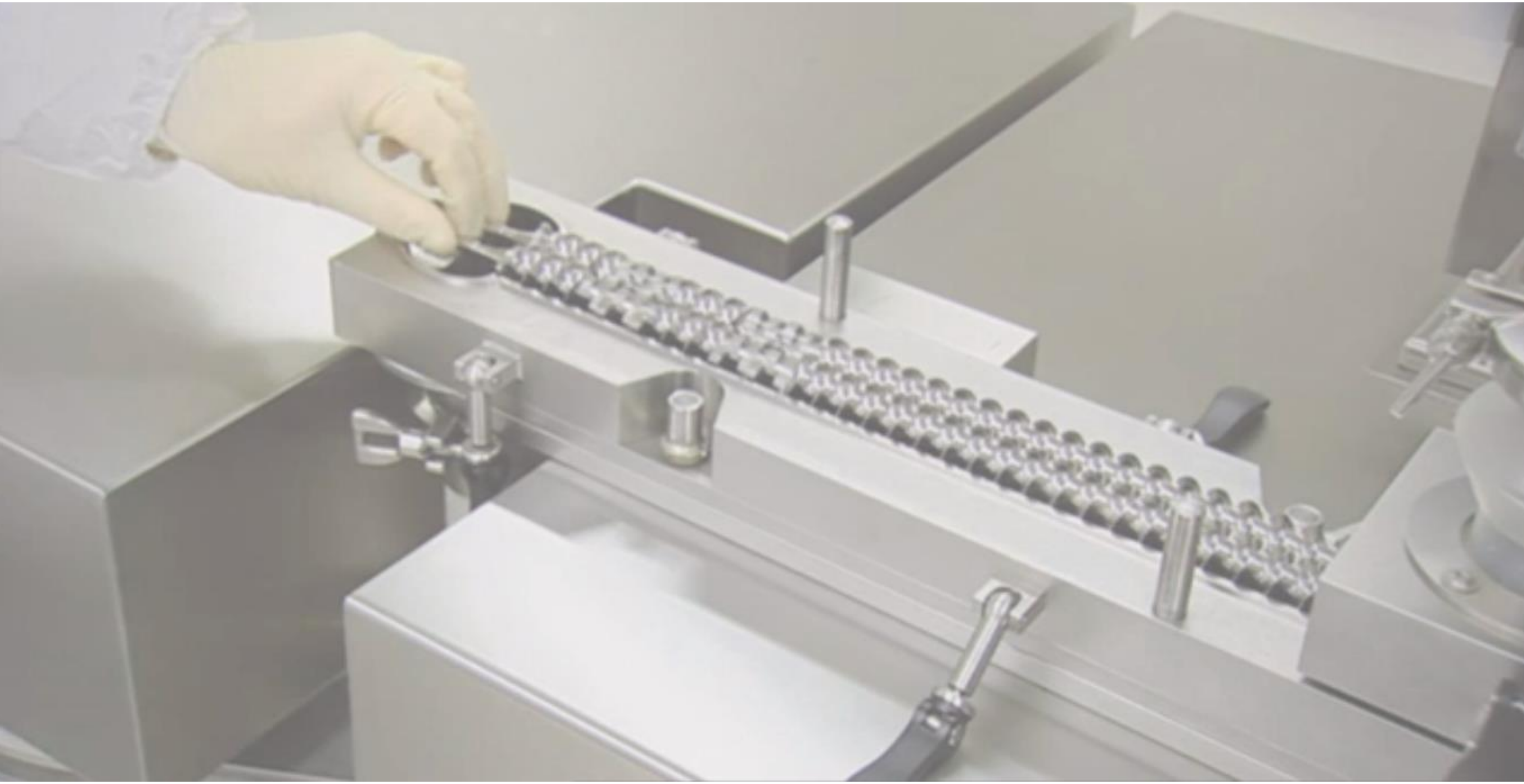
Key questions for twin-screw granulation process development

What affects granulation time and mixing?

What control degree of rate processes involved in desired quality of granules?

Consigma™-1 system
(GEA pharma systems, Collette)

Open barrel of a twin screw granulator

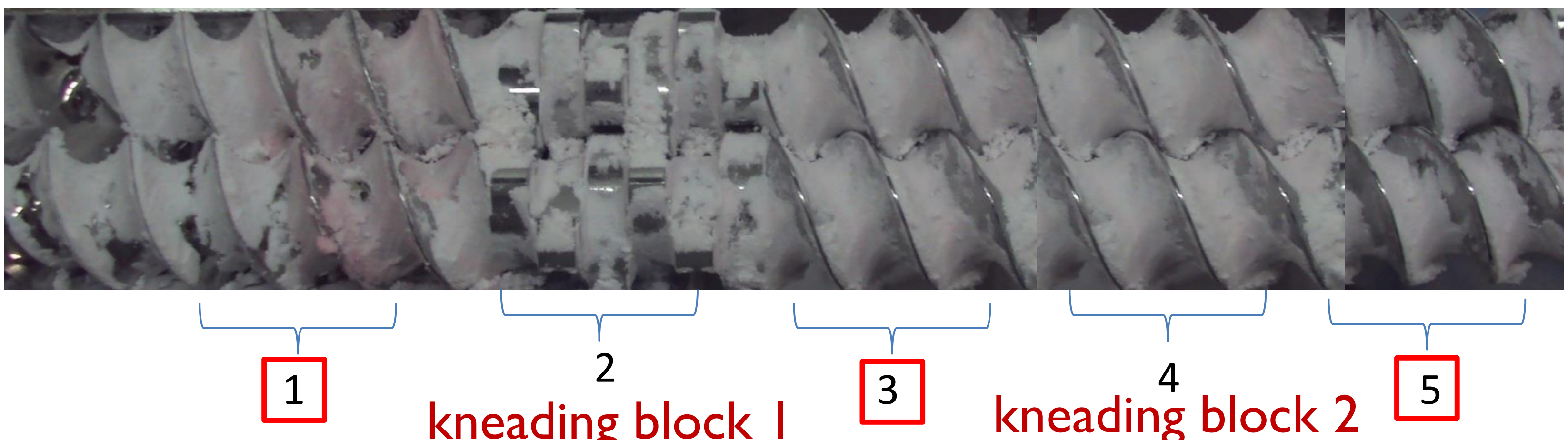


Consigma - 1 experiments

Lactose/PVP (97.5/2.5) premix was granulated with distilled water

Factors:

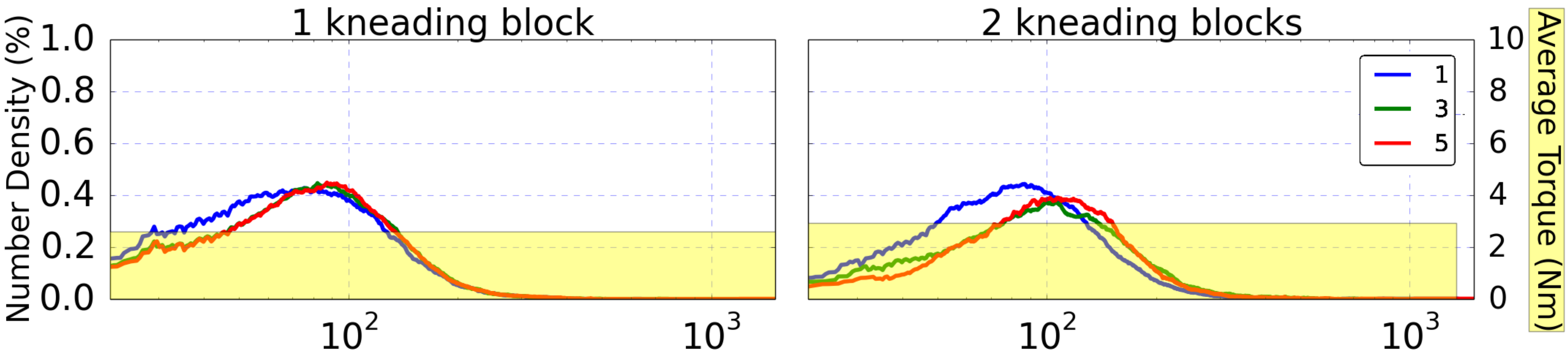
Parameters	Low	High
Throughput	10 Kg/h	25 Kg/h
Liquid-solid ratio	4.58 %	6.52%
Screw speed	500 RPM	900 RPM



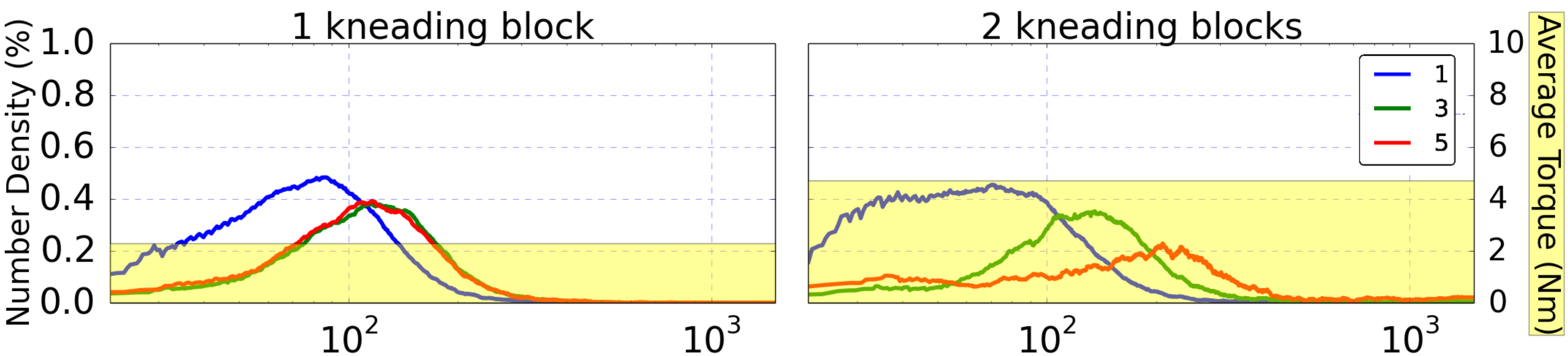
Responses: Particle characterization by Laser Obscuration Time technique (Location 1, 3, 5)

Comparing average Feret diameter

Throughput Low	Liquid-solid ratio Low	Screw speed Low



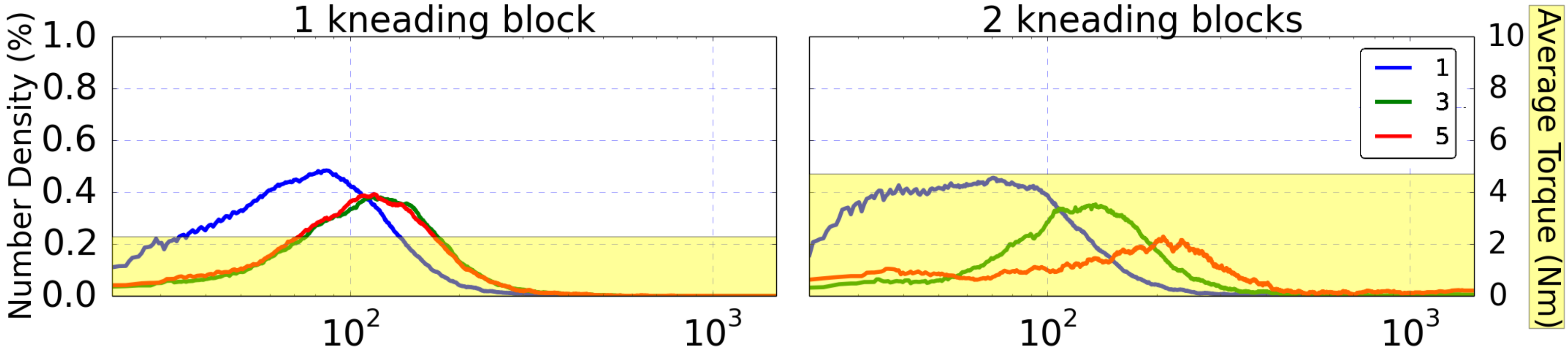
Throughput High	Liquid-solid ratio High	Screw speed Low



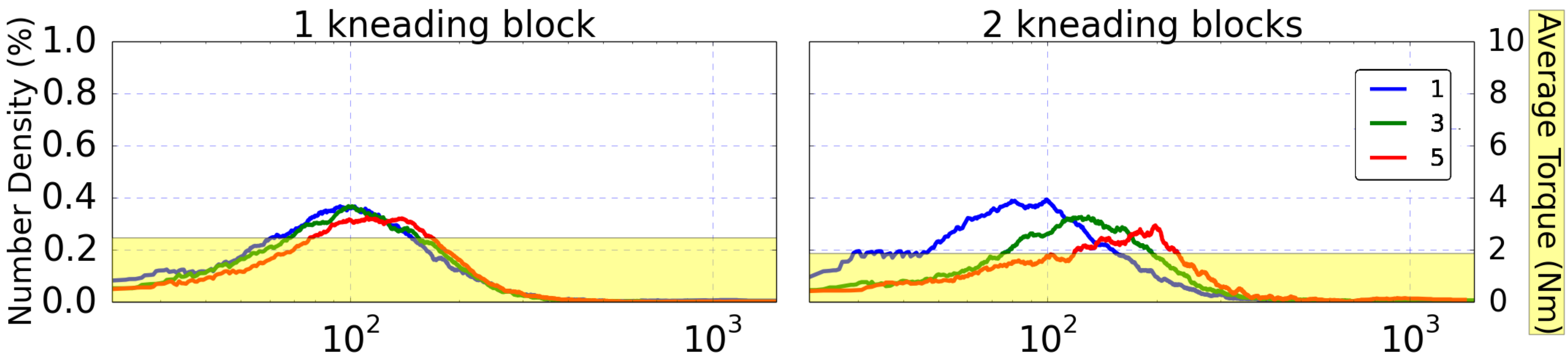
Comparing average Feret diameter

At high Throughput and L/S

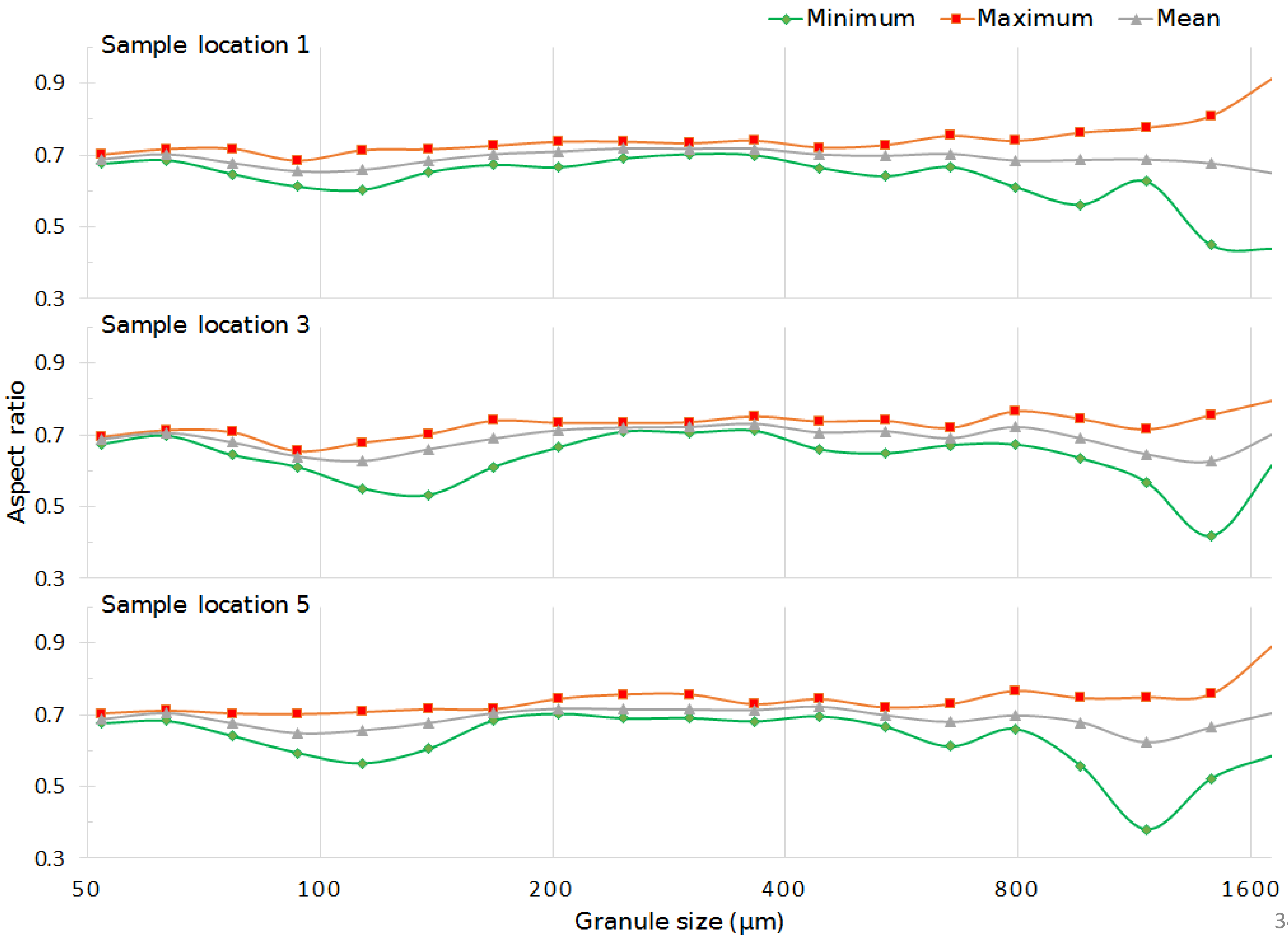
Throughput High	Liquid-solid ratio High	Screw speed Low



Throughput High	Liquid-solid ratio High	Screw speed High



Average Feret diameter vs Aspect ratio



Population balance equation

$$\frac{\partial n}{\partial t}+\nabla\cdot\left(\mathbf{u}_p n\right)-\nabla\cdot\left(D_p\nabla n\right)=$$

Granule size distribution

$$N\,\delta(V-v_o)-\frac{\partial}{\partial V}(G\,n)$$

Nucleation and growth term

$$+\frac{1}{2}\int_0^V \beta(v,V-v)\,n(v)\,n(V-v)\,dv-n(V)\int_0^\infty \beta(v,V)\,n(v)\,dv$$

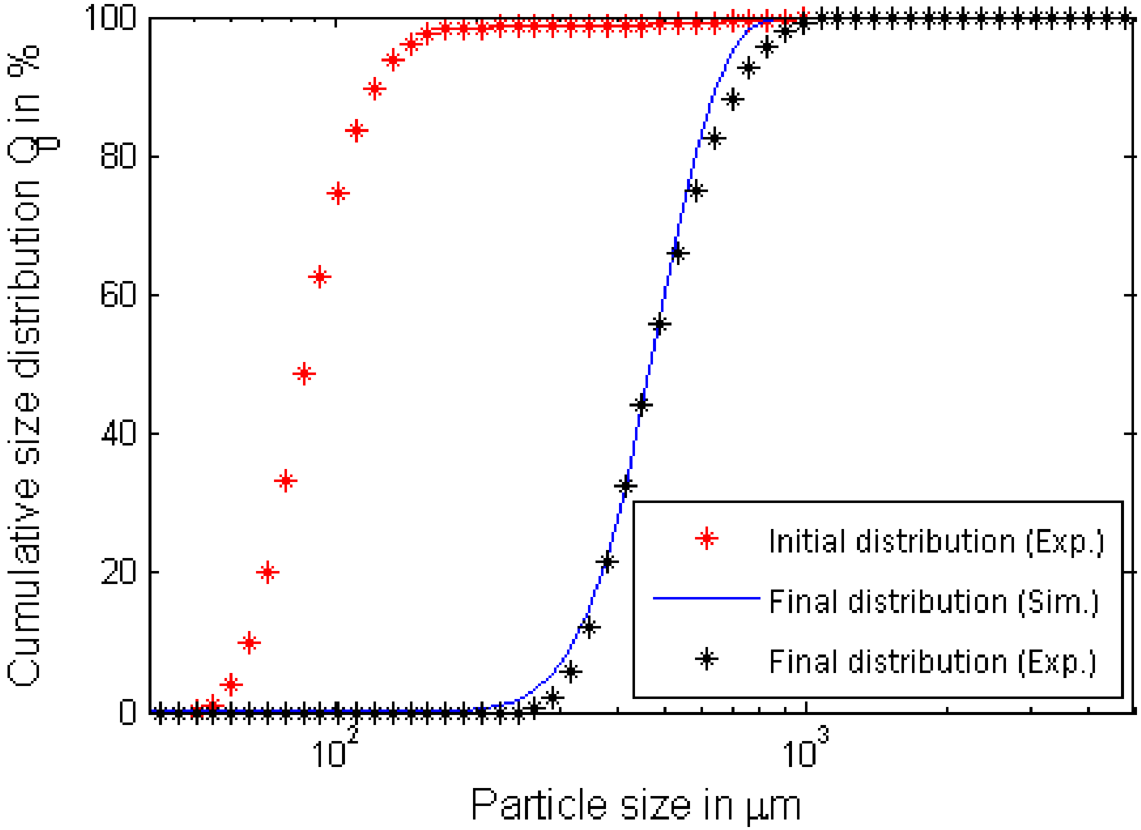
Aggregation term

$$+\int_V^\infty \Gamma(\Phi)\,b(V;\Phi)\,n(\Phi)\,d\Phi-\Gamma(V)\,n(V)$$

Breakage term

N = nucleation rate
G = growth rate
β = aggregation rate
Γ = breakage rate
b = daughter distribution
v_o = nuclei size

Ignoring effect of granulator design on granule size distribution

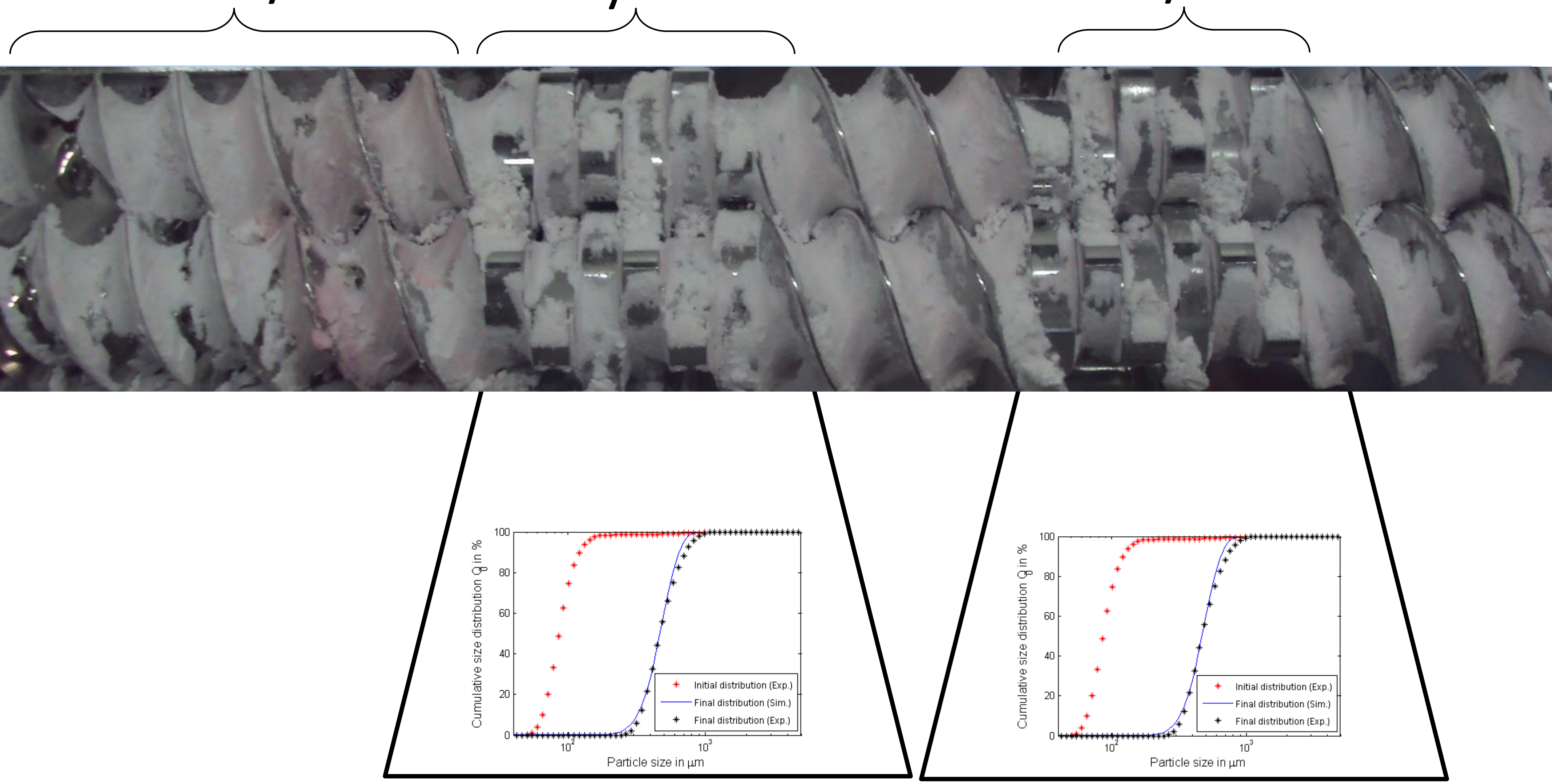


Multiple factors contribute to the variation in granule size distribution

Partially filled

Fully filled

Fully filled



Conclusions

Along with experimental study, an improved insight can be obtained by model-based analysis

(as we already seen in case of RTD).

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

High throughput can easily be achieved by simultaneously increasing the feed rate and screw speed.

What next…

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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BIOMATH

Model-based analysis and optimization of bioprocesses

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