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Experimental and model-based investigation of twin screw granulation: towards more profound process knowledge

Ashish Kumar

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LABORATORY OF PHARMACEUTICAL PROCESS ANALYTICAL TECHNOLOGY
FACULTY OF PHARMACEUTICAL SCIENCES
BIOMATH, DEPARTMENT OF MATHEMATICAL MODELLING, STATISTICS AND BIOINFORMATICS
FACULTY OF BIOSCIENCE ENGINEERING

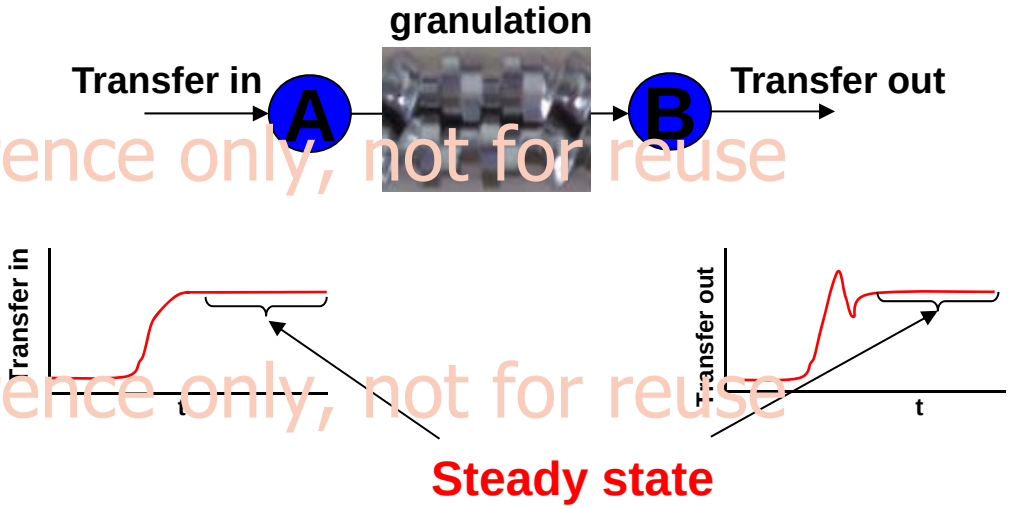
Continuous manufacturing line
Consigma™-25 system

Continuous twin-screw granulator

Segmented Fluid bed dryer

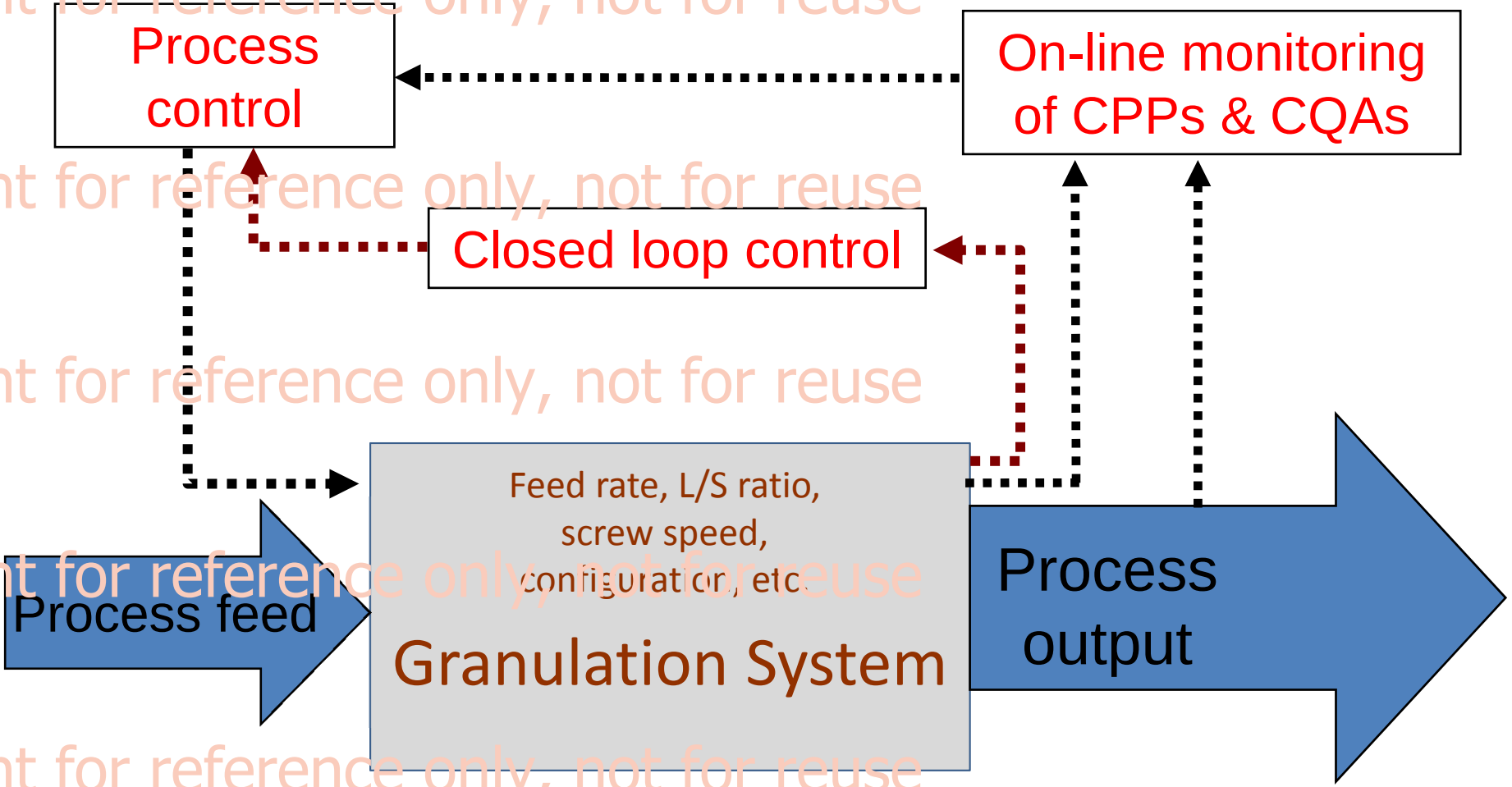
Granule conditioning module

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

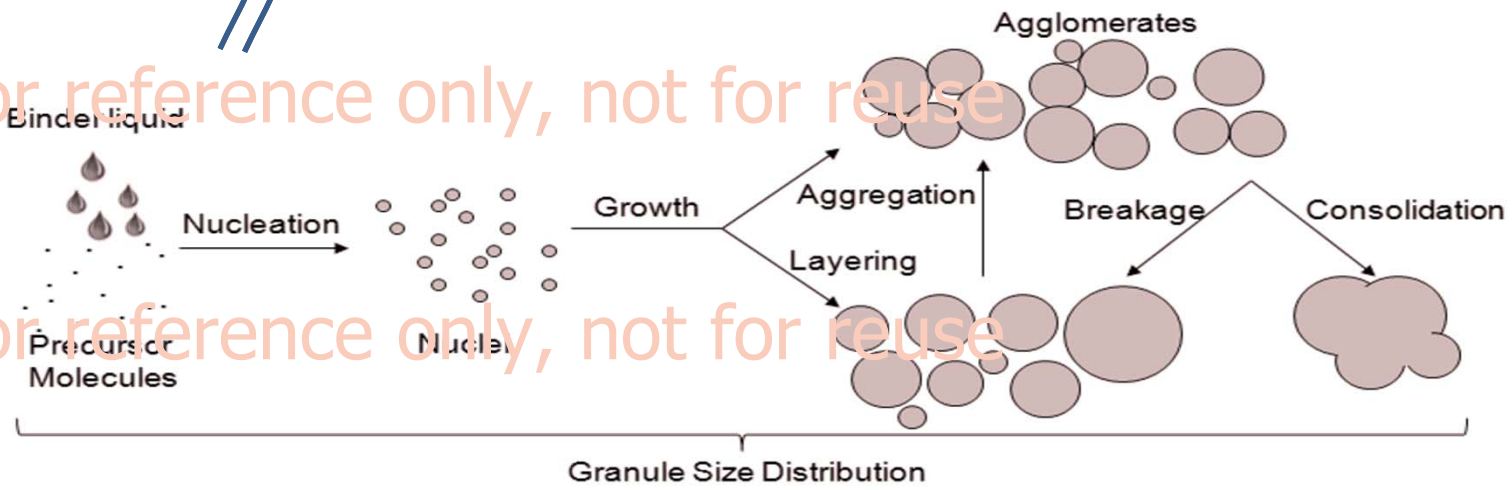


Two key implications

1. Fluxes are roughly constant (Dynamics are transient)
2. If feed is constant, product quality is consistent!



Twin-Screw Granulator applies High Shear Wet Granulation

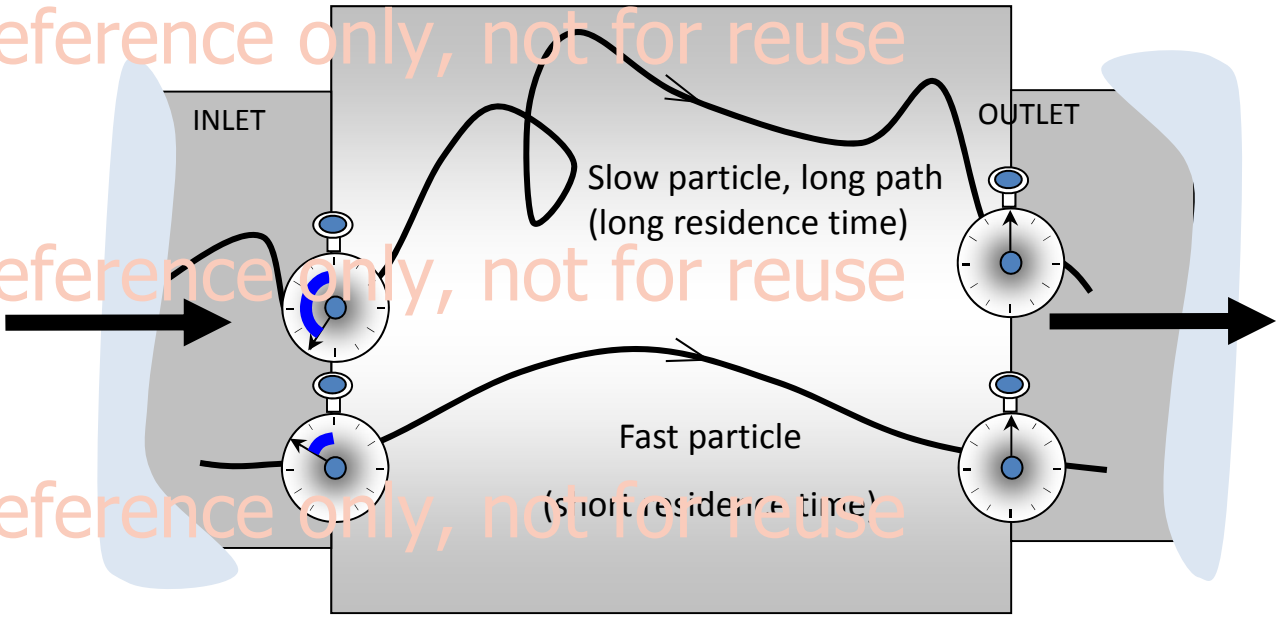


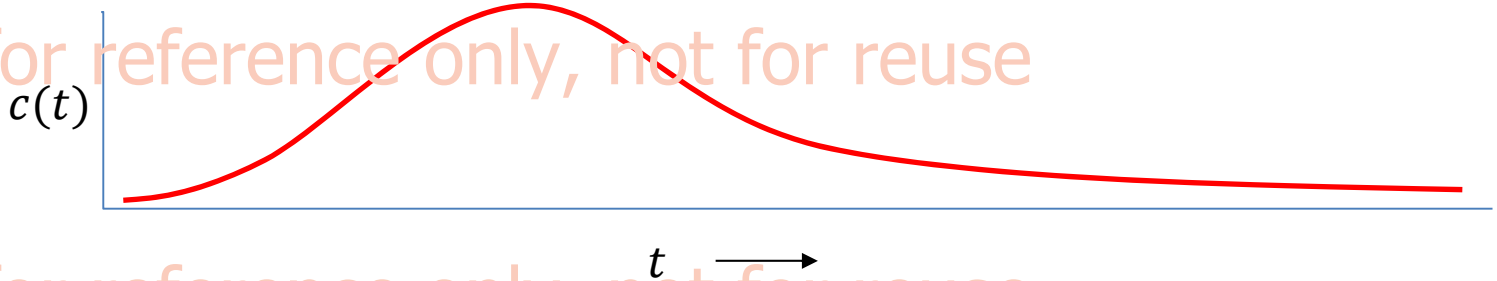
Key questions for twin-screw granulation process development

Which parameters affect granulation time and mixing?

Which parameters affect aggregation and breakage rates?

Residence time distribution to know the granulation time and mixing

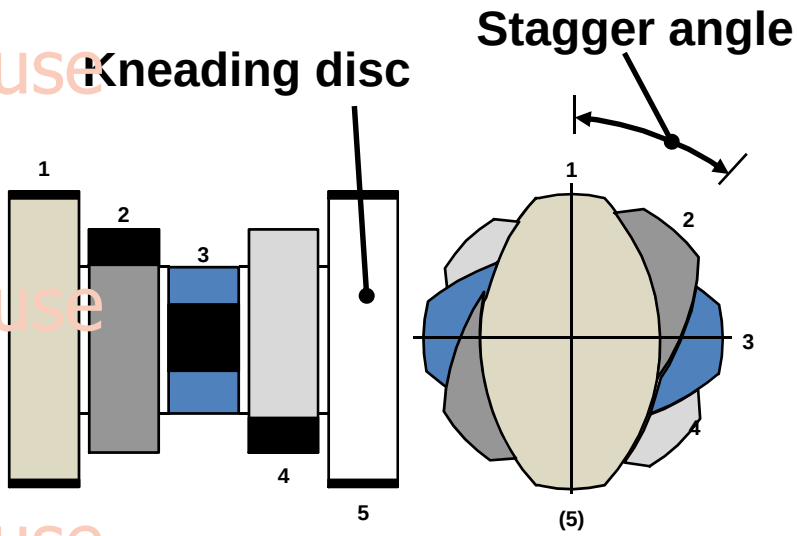




Residence time distribution to know the granulation time and mixing

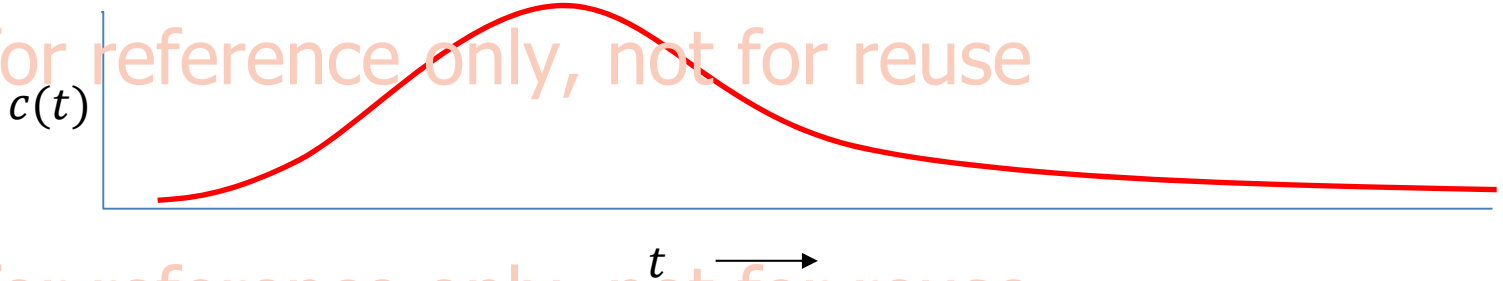
Screw configuration

- Number of kneading discs
- Stagger angle

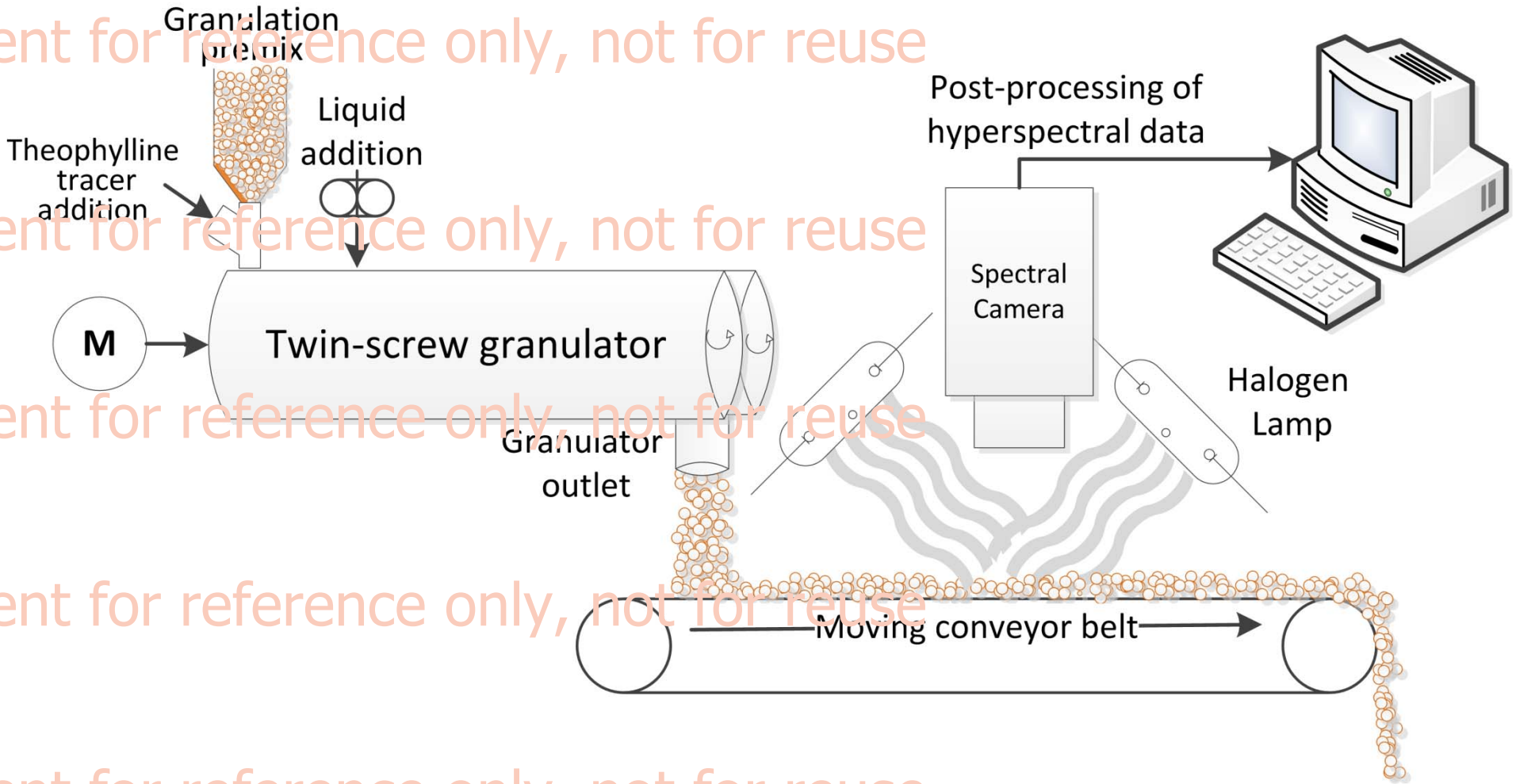


Process parameters

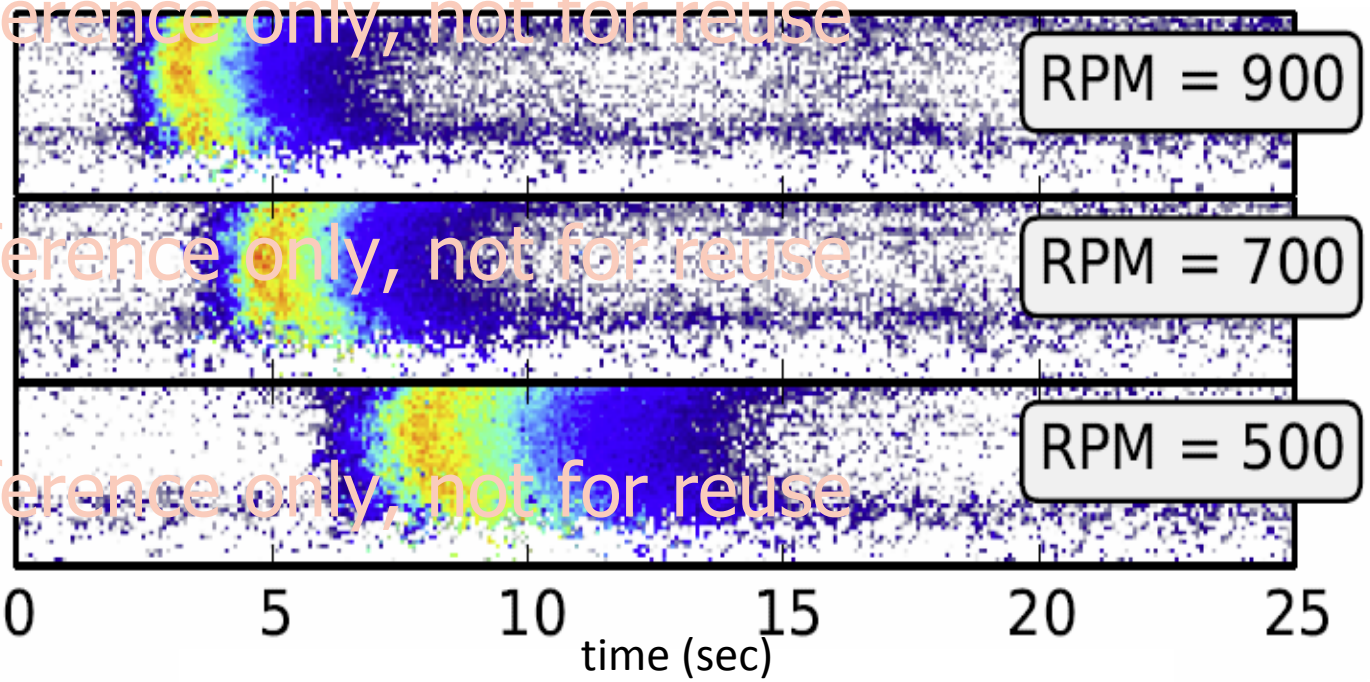
- Material throughput
- Screw speed

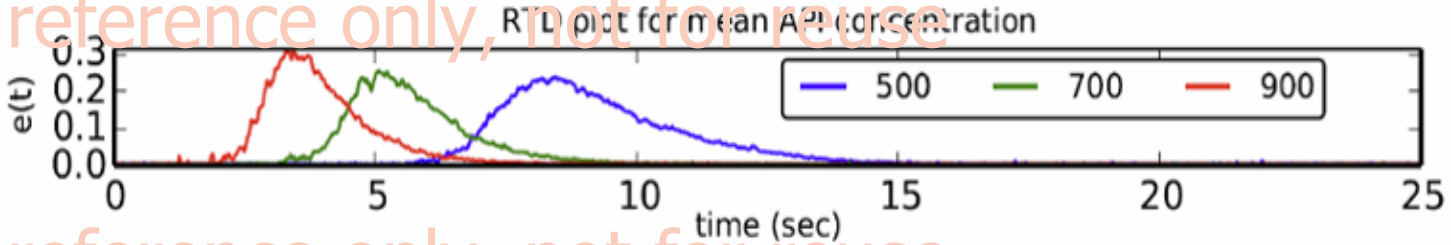


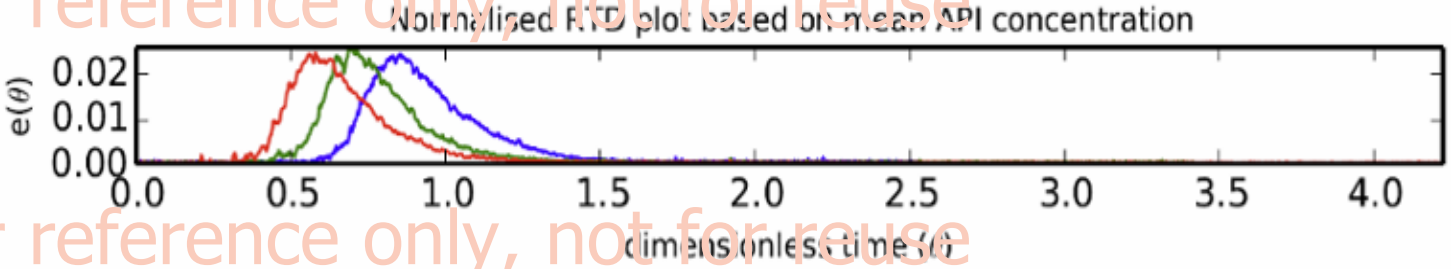
Tracer concentration in granules produced was measured using NIR chemical imaging



API Map was used to measure RTD







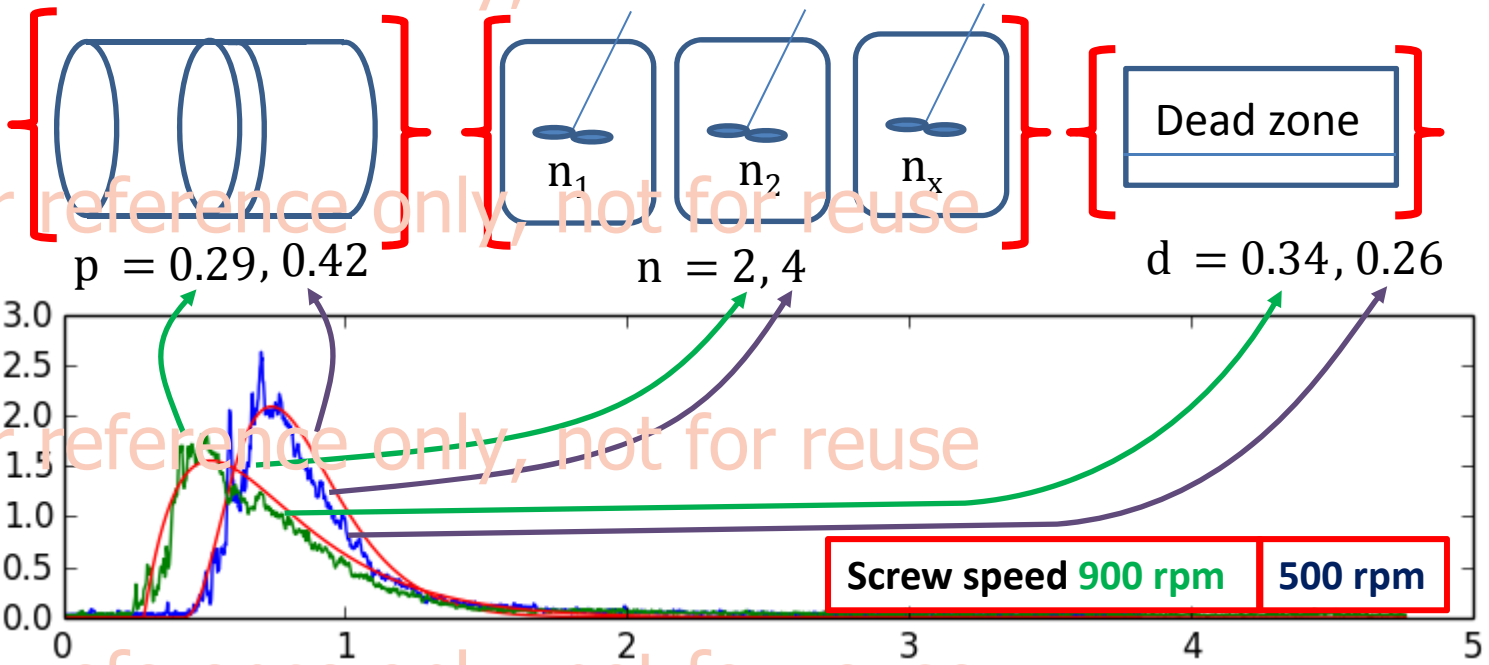
Conceptual model to include three main components of RTD

Modified Tank-in-Series model used

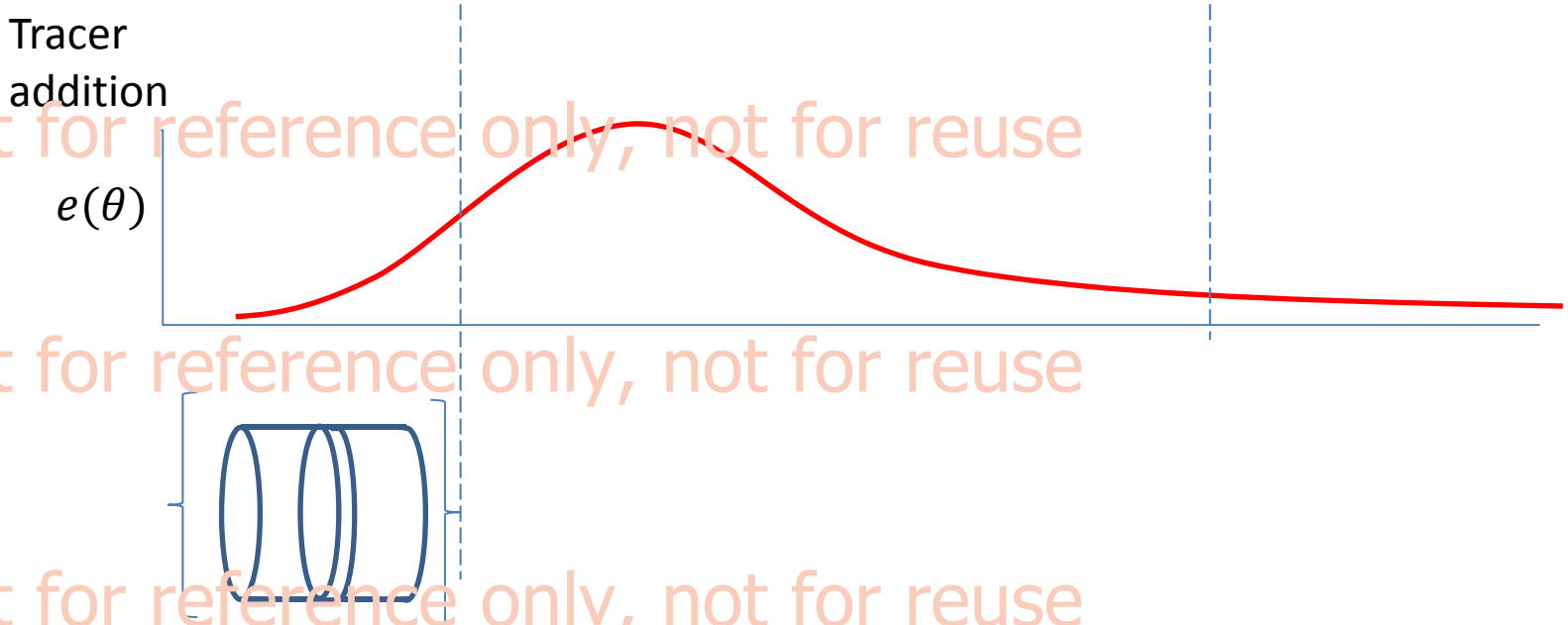
Modified Tank-In-Series model

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

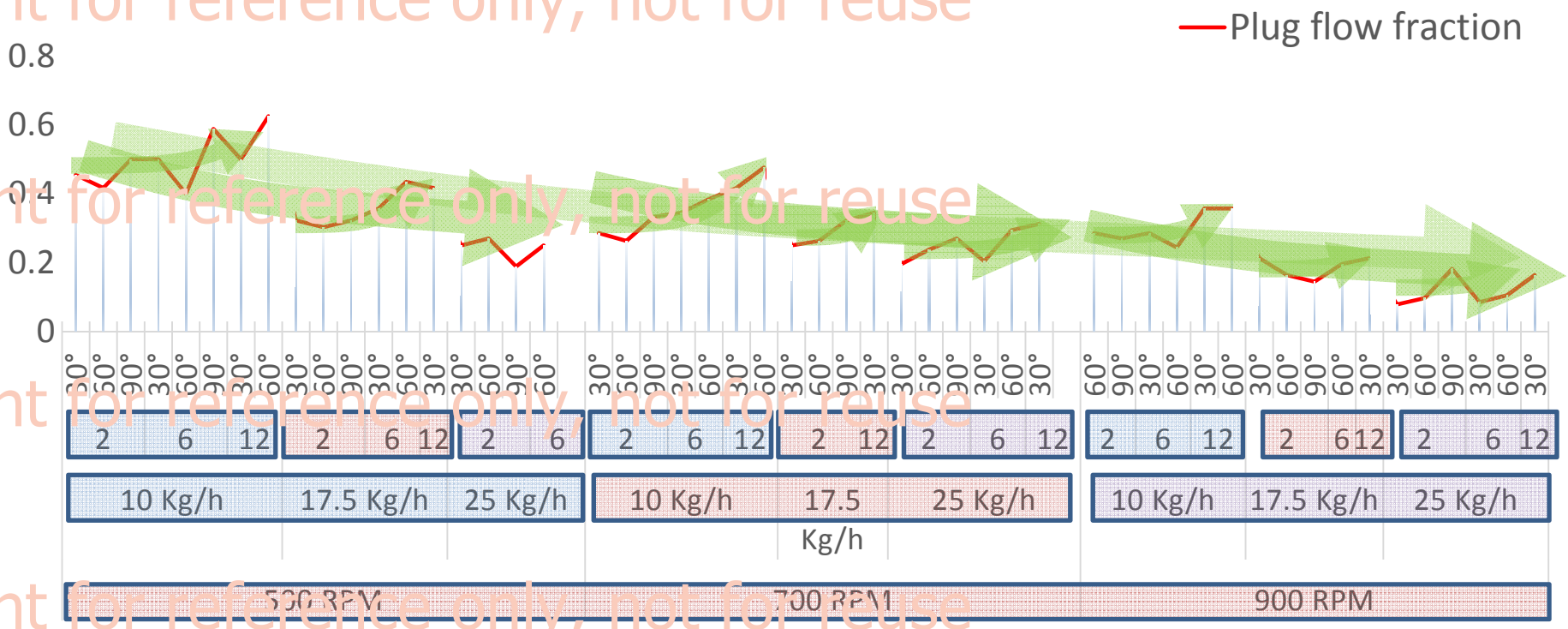
where, $b = \frac{n}{(1-p)(1-d)}$



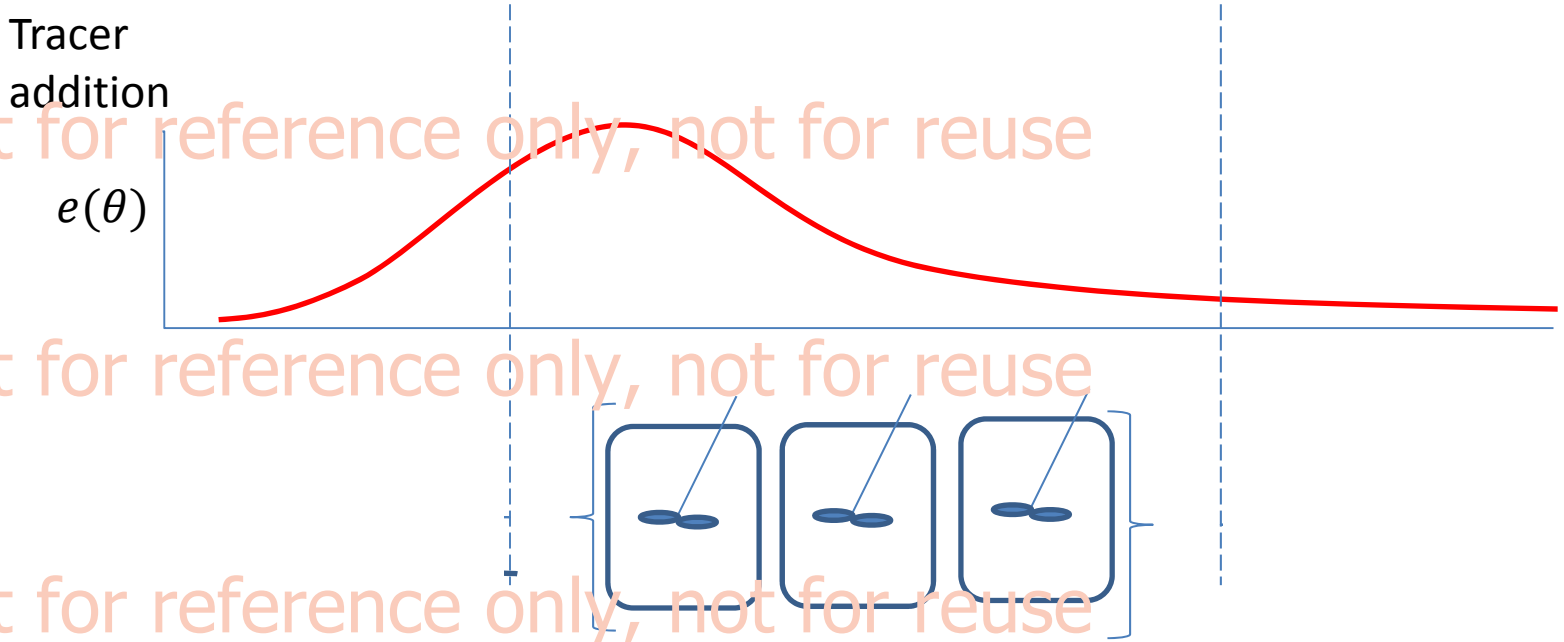
Plug flow component of the RTD



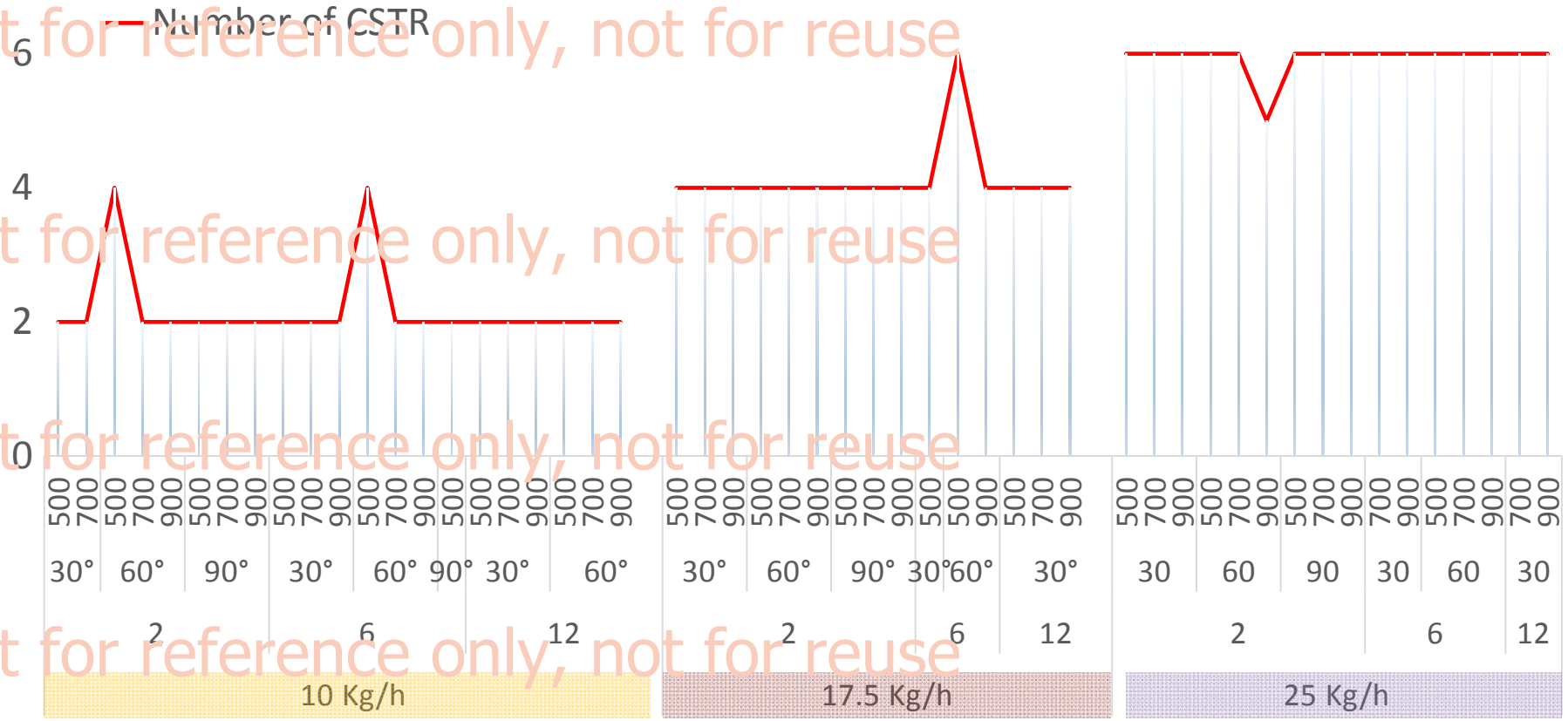
Plug flow fraction decreases with increase in screw speed and throughput



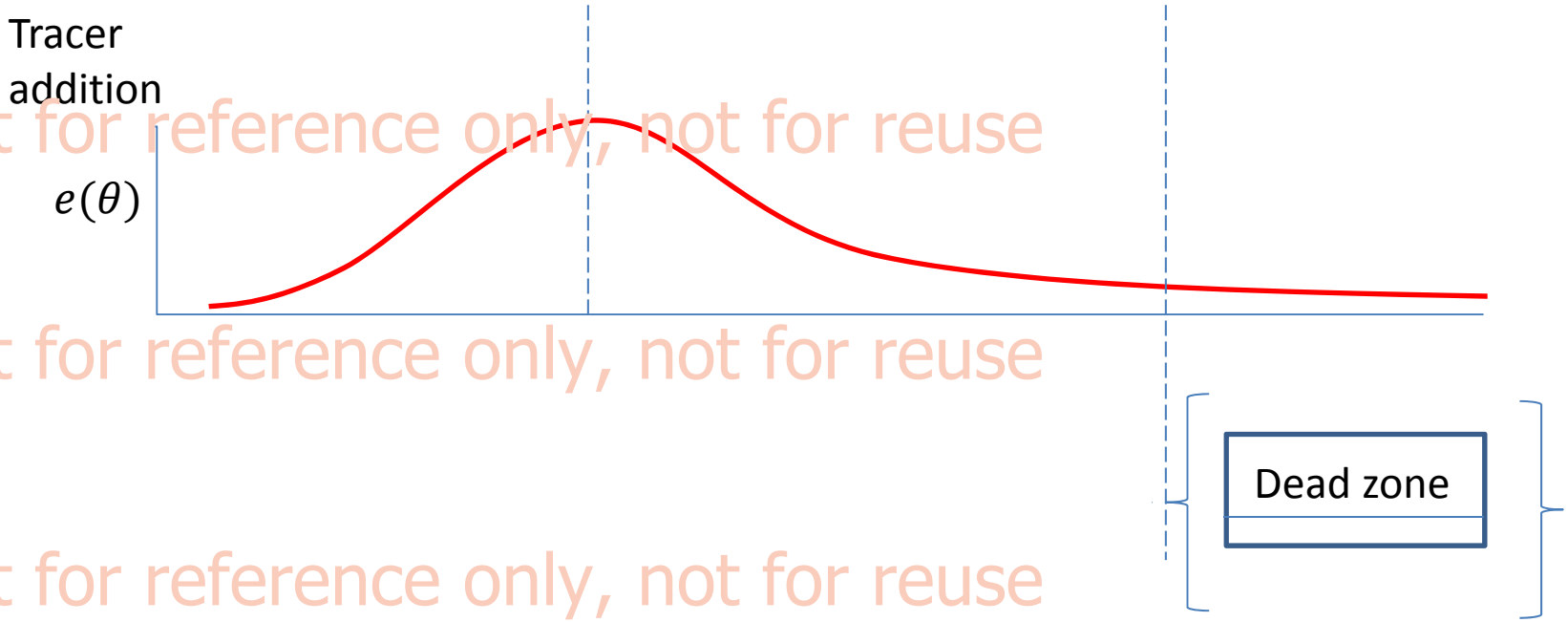
Mixed flow component of the RTD



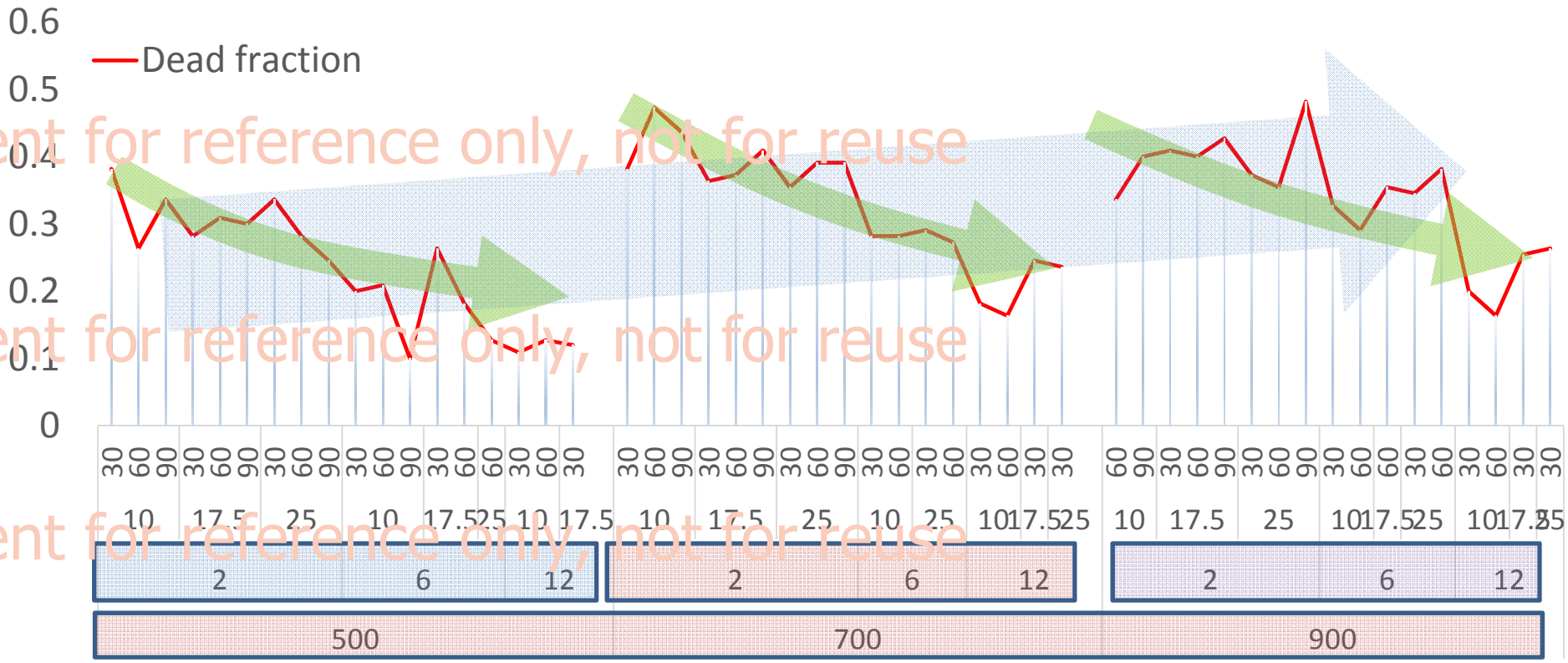
Material throughput controls mixing which reduces with increase in throughput



Mixed flow component of the RTD



Dead zone increases with screw speed, and reduces with number of kneading discs



RTD analysis showed that

Kneading blocks primarily act as plug-flow zones.

Kneading zone prevents excessive back mixing in the granulator.

Material throughput dominantly controls mixing.

Key questions for twin-screw granulation process development

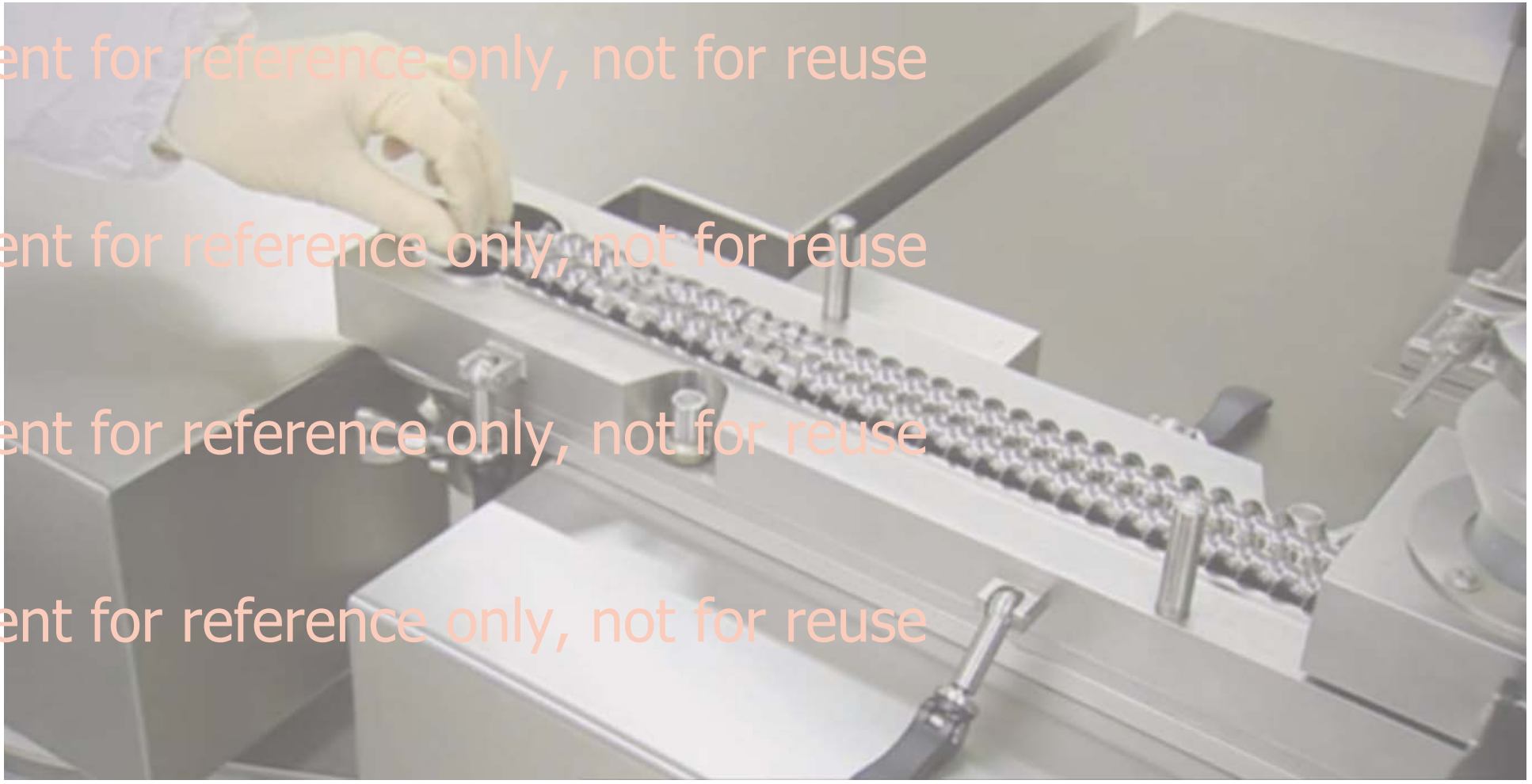
Which parameters affect granulation time and mixing?

Which parameters affect aggregation and breakage rates?

Consigma™-1 system

(GEA pharma systems, Collette)

Open barrel of a twin screw granulator

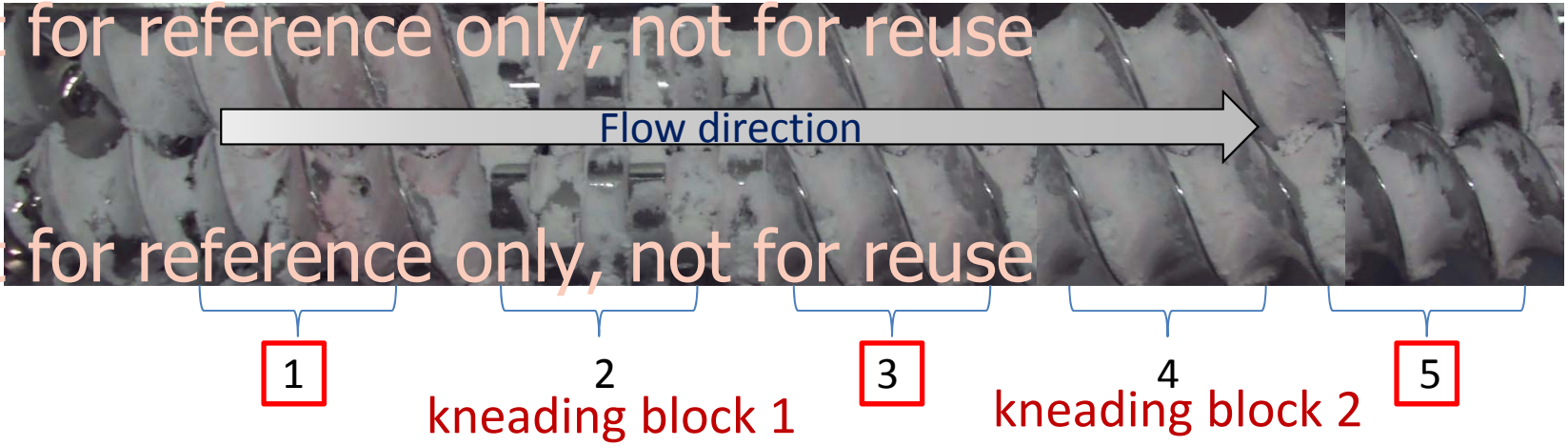


Consigma™- 1 experiments

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

Factors:

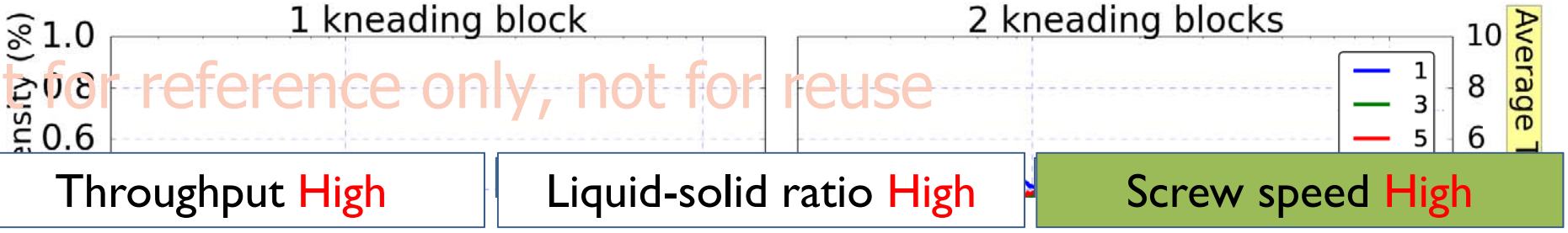
Parameters	Low	High
Throughput	10 Kg/h	25 Kg/h
Liquid-solid ratio	4.58 %	6.52%
Screw speed	500 RPM	900 RPM



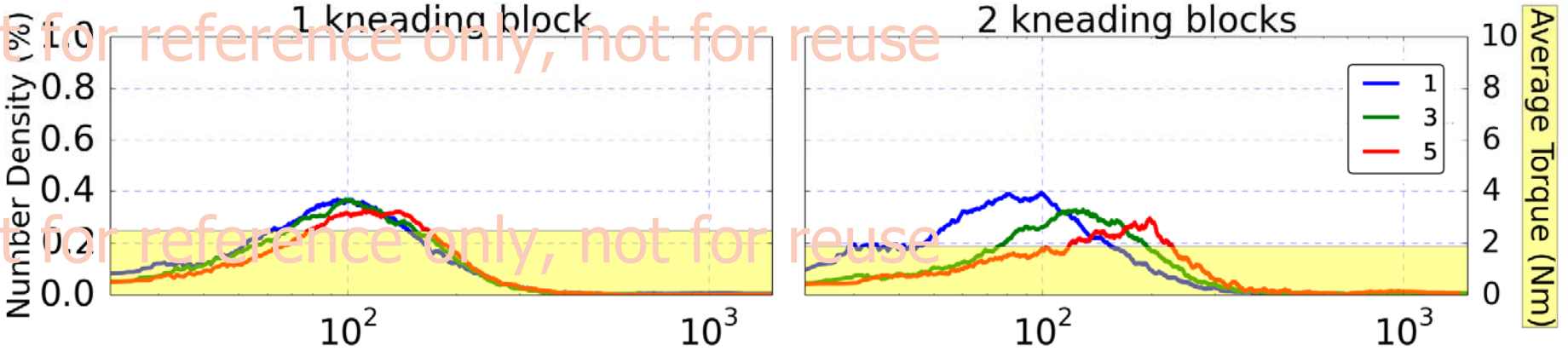
Responses: Particle characterization by Dynamic Image Analysis (Location 1, 3, 5)

Comparing average Feret diameter

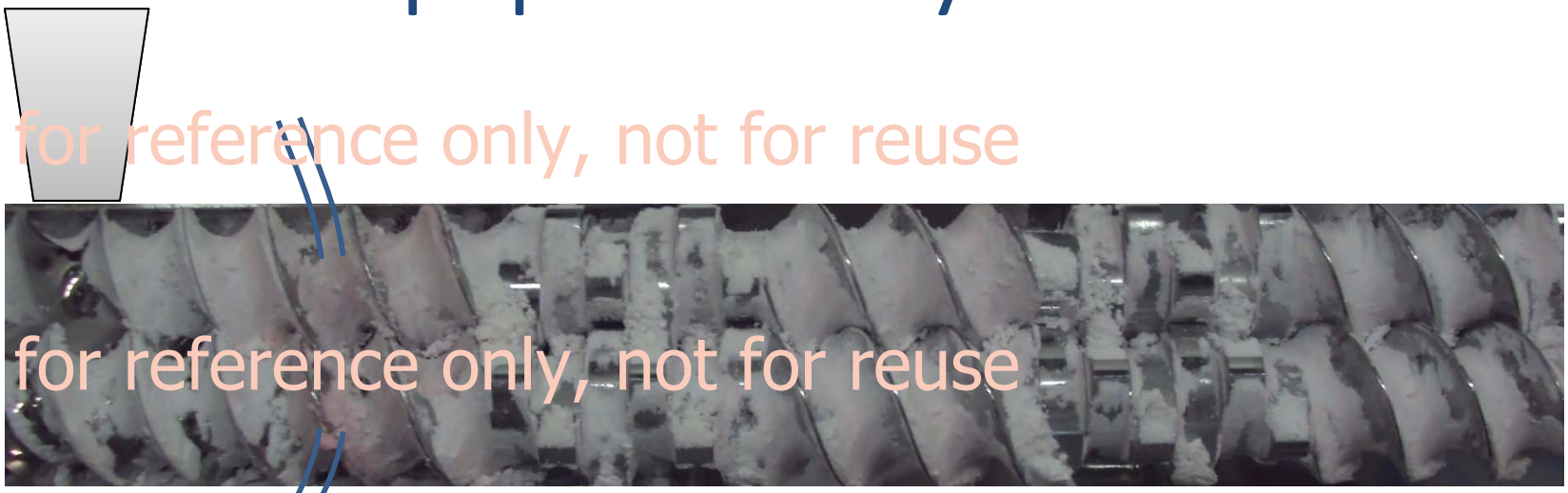
Throughput Low | Liquid-solid ratio Low | Screw speed Low

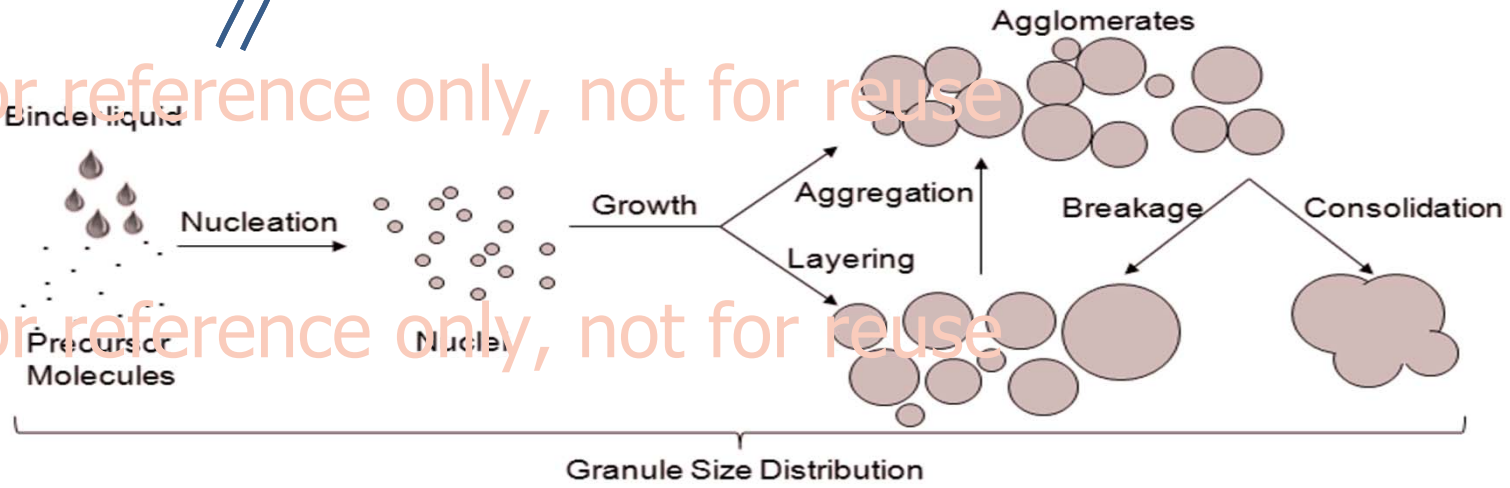


Throughput High | Liquid-solid ratio High | Screw speed High



Granulation is result of particle population dynamics





Population balance equation

$$\frac{\partial n(t,x)}{\partial t} = \frac{Q_{in}}{\tilde{V}} n_{in}(x) - \frac{Q_{out}}{\tilde{V}} n_{out}(x)$$

GSD balance

Aggregation term

$$+\frac{1}{2}\int_0^x \beta(t, x-\varepsilon, \varepsilon)\, n(t, x-\varepsilon)\, n(t,\varepsilon)\, d\varepsilon$$

$$-n(t,x)\int_0^\infty \beta(t,x,\varepsilon)\, n(t,\varepsilon)\, d\varepsilon$$

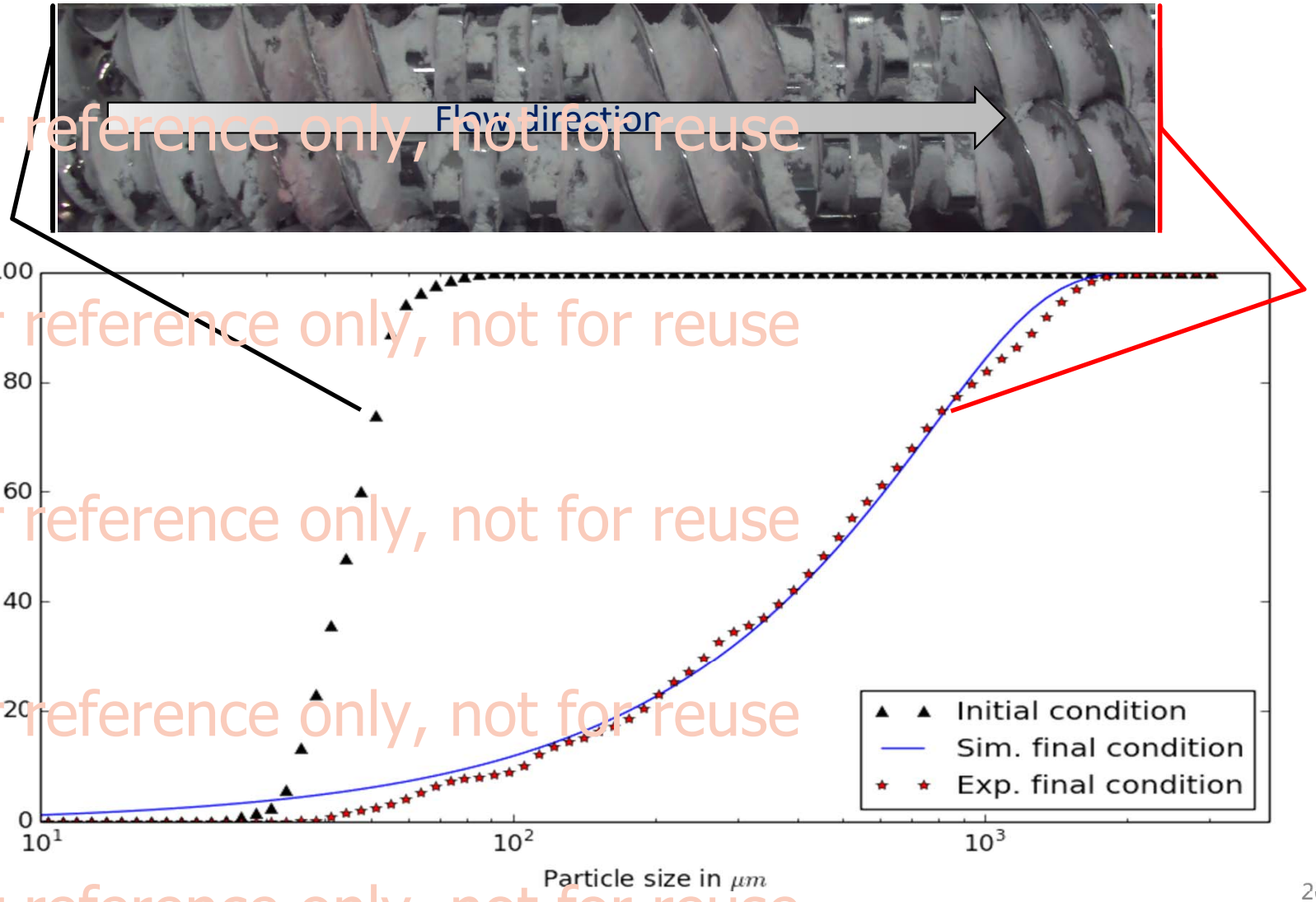
Breakage term

$$+\int_0^\infty b(x,\varepsilon) S(\varepsilon) n(t,\varepsilon)\, d\varepsilon$$

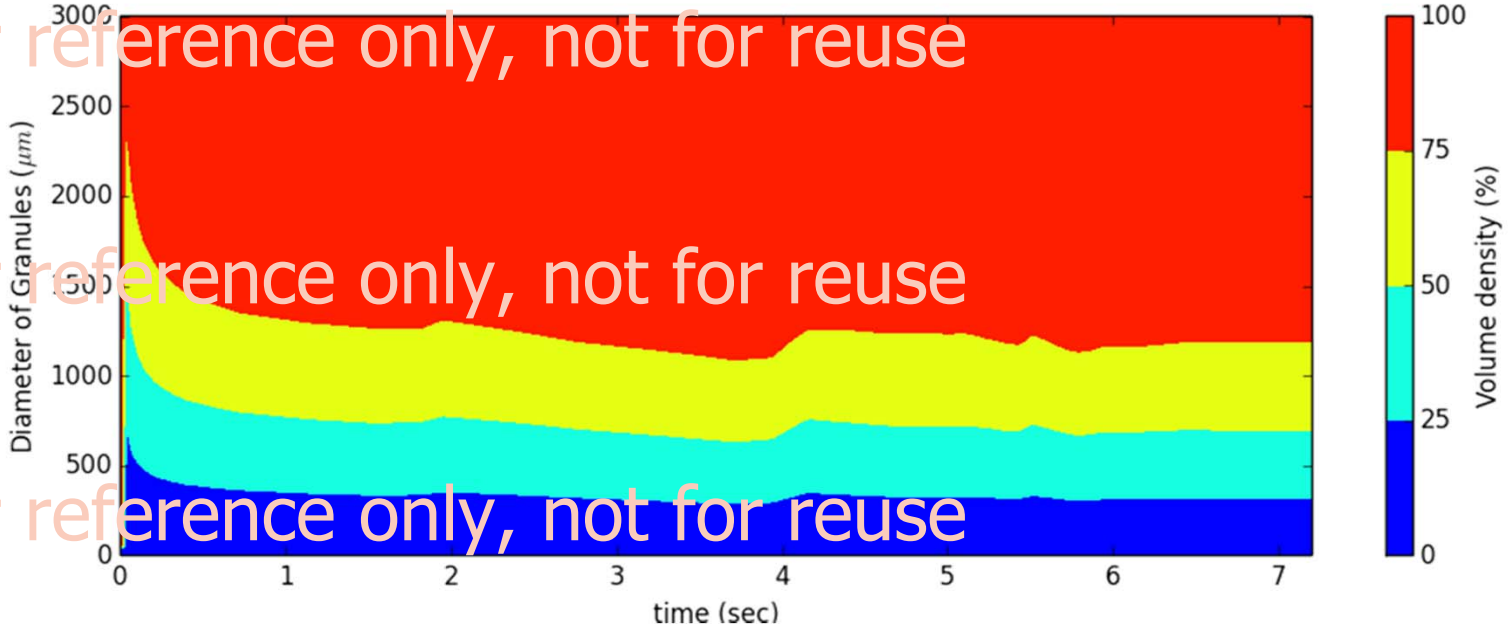
$$-S(x) n(t,x)$$

β = aggregation rate
S = selection rate
b = breakage function

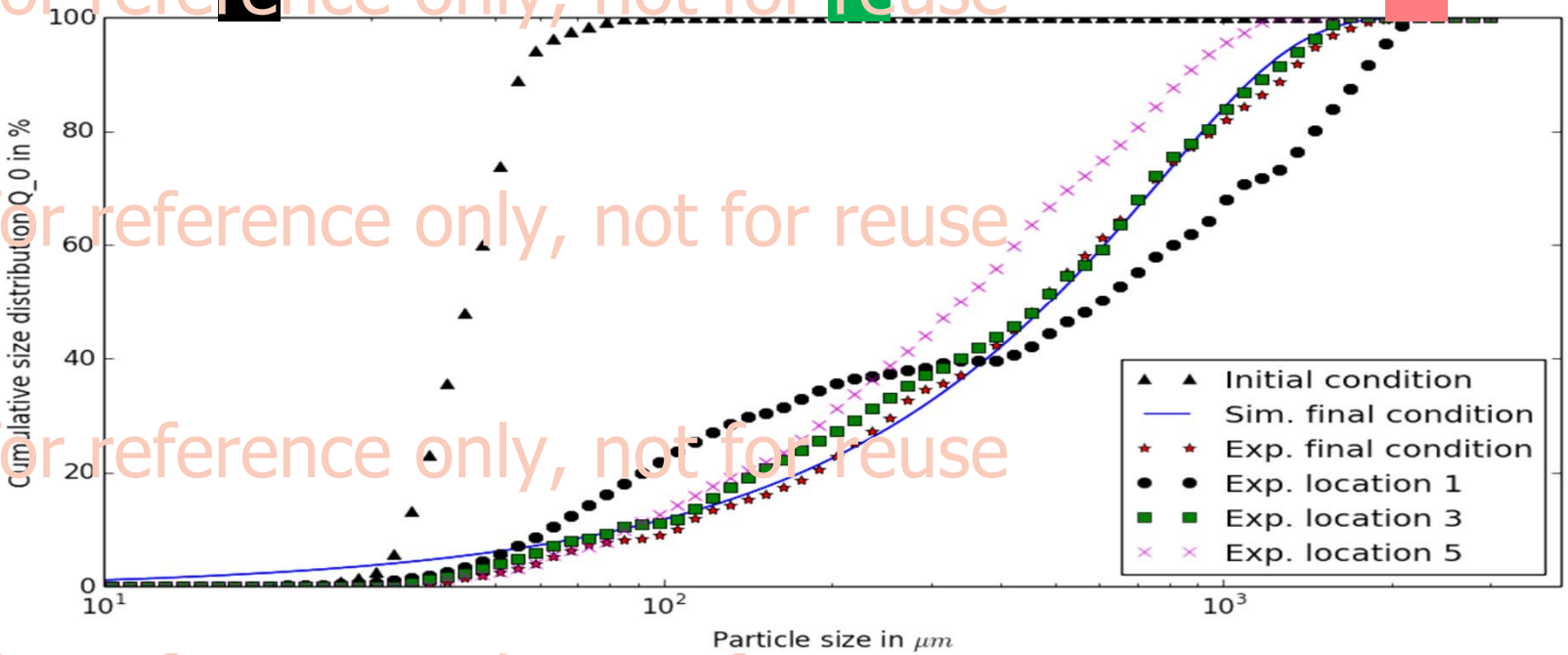
Experimental and simulated data have a good agreement



Particle population dynamics during granulation



Including effect of granulator design on granule size distribution



Conclusions

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

Kneading blocks act as plug-flow zones in TSG, while the material throughput controls mixing.

High throughput can be achieved by increasing the liquid-solid ratio and screw speed.

PBM requires further development to include screw geometry effect in twin-screw granulation.

Prof. Ingmar Nopens
Prof. Thomas De Beer
Prof. Krist V. Gernaey

Jurgen Vercruysse
Valérie Vanhoorne

Maunu Toiviainen
Panouillot Pierre-Emmanuel
Mikko Juuti

Kris Schoeters

UNIVERSITEIT GENT

Laboratory of Pharmaceutical Process Analytical Technology

BIOMATH

Model-based analysis and optimization of bioprocesses

Ashish.Kumar@UGent.be