

Experimental and model-based investigation of twin screw granulation

Ashish Kumar

Kuopio Summer School, 19 October, 2015

LABORATORY OF PHARMACEUTICAL PROCESS ANALYTICAL TECHNOLOGY

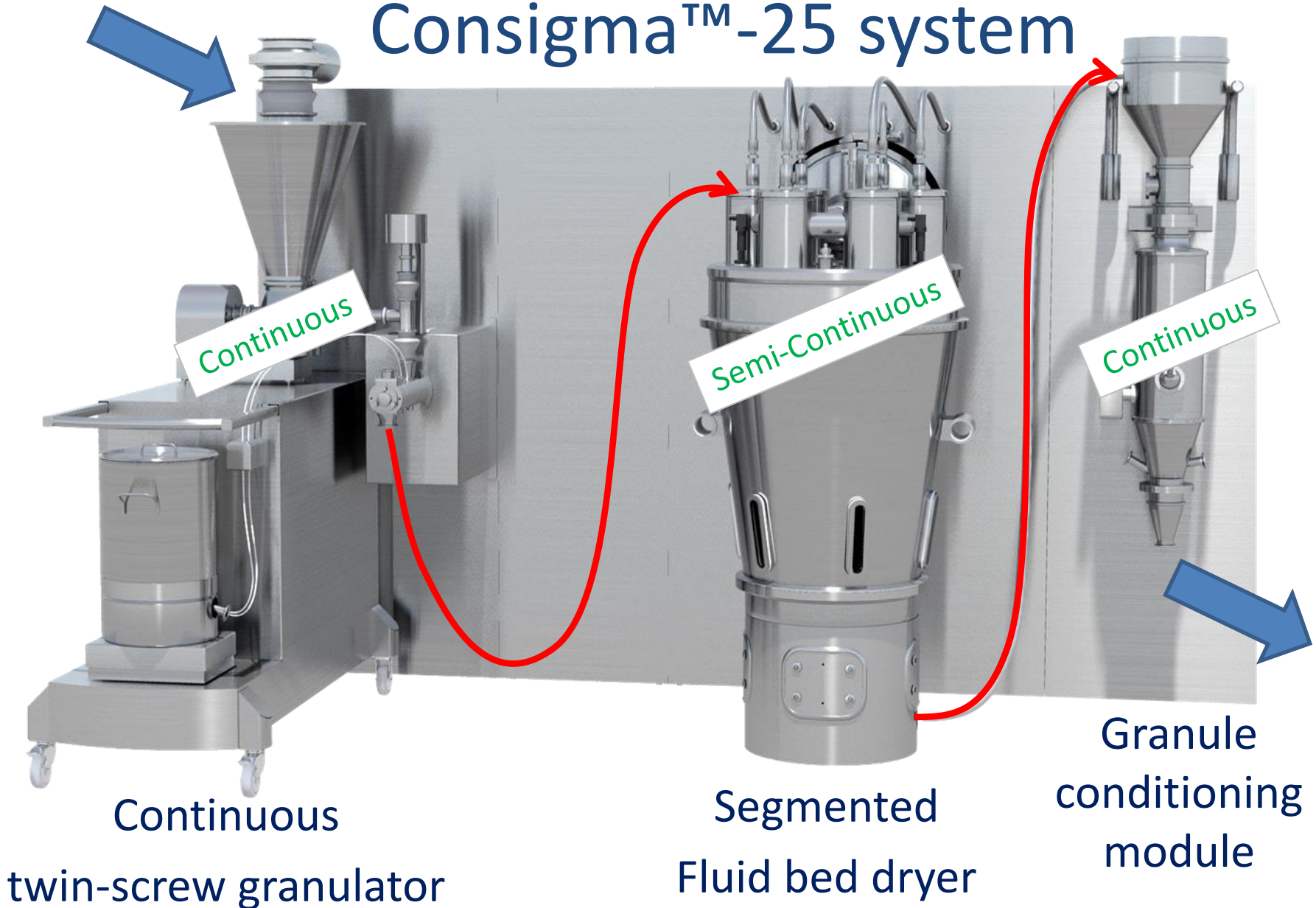
FACULTY OF PHARMACEUTICAL SCIENCES

BIOMATH, DEPARTMENT OF MATHEMATICAL MODELLING, STATISTICS AND BIOINFORMATICS

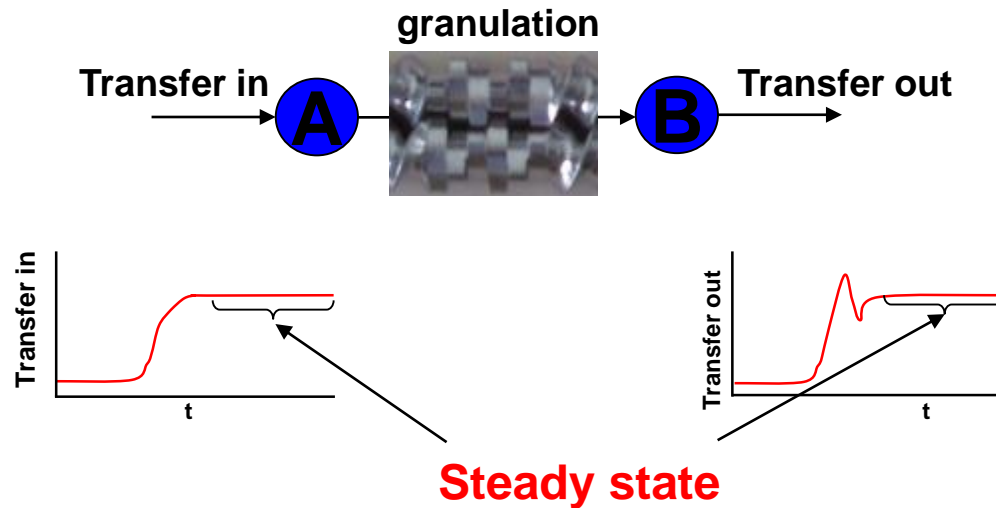
FACULTY OF BIOSCIENCE ENGINEERING

Continuous manufacturing line

Consigma™-25 system

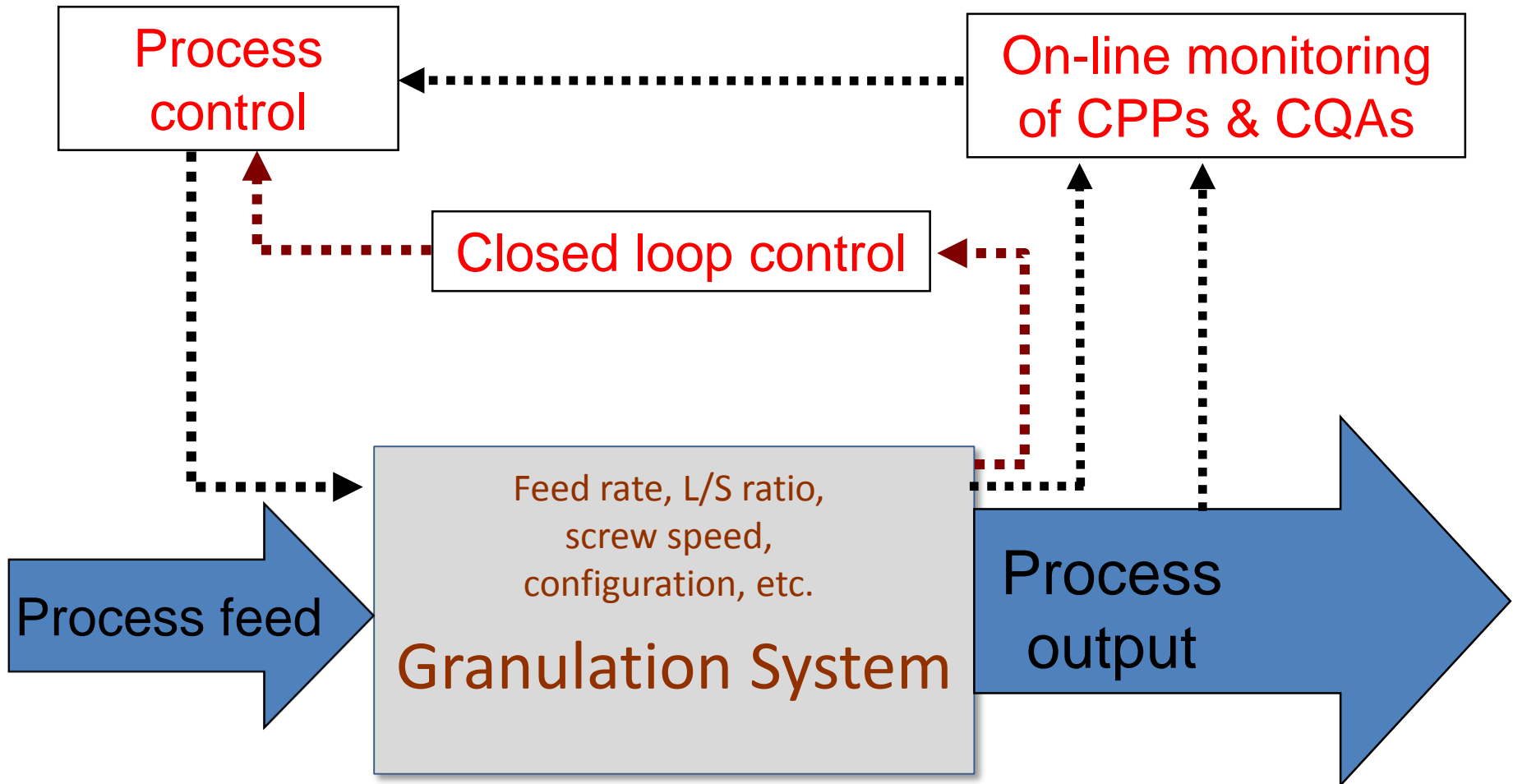


At appropriate time-scales and conditions, granulation is in steady state

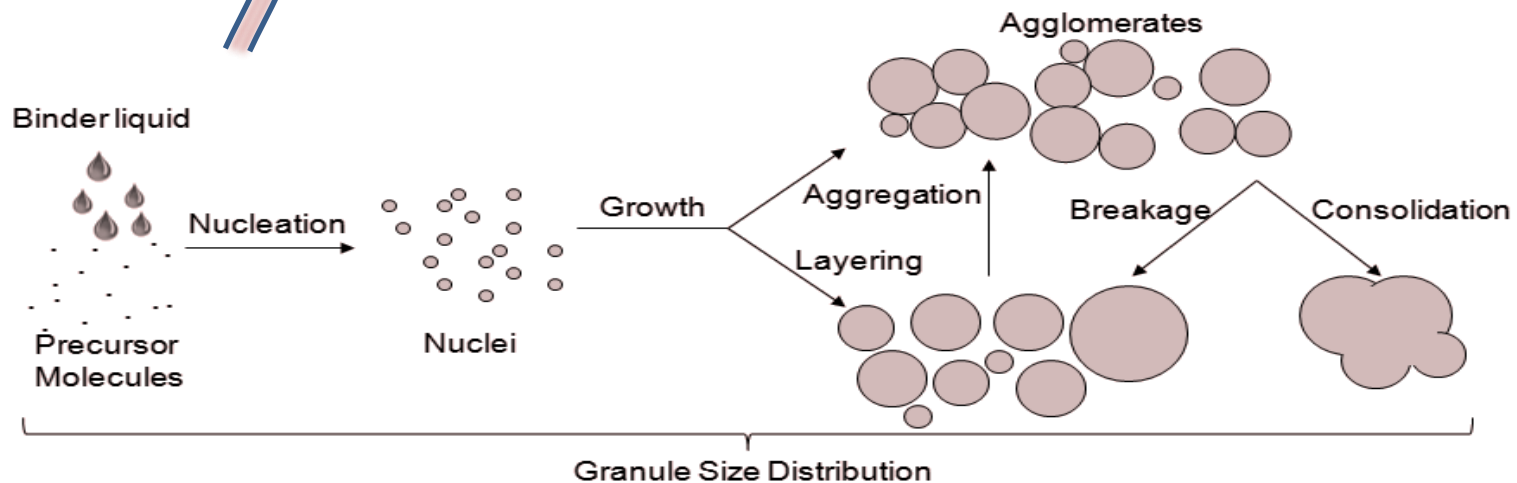
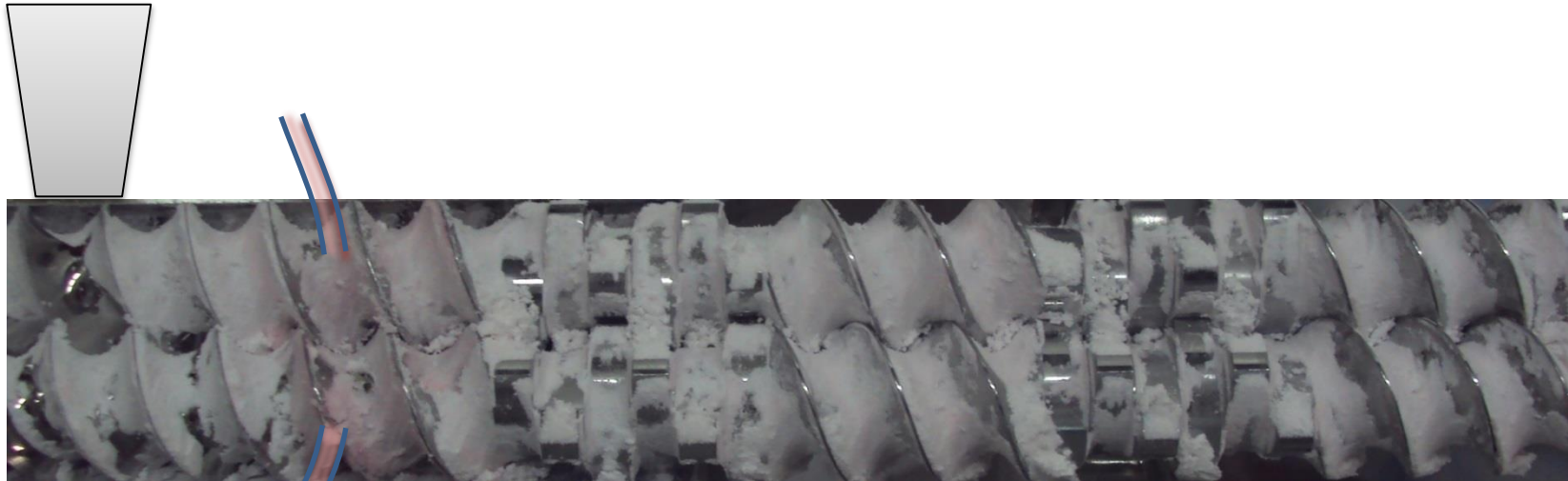


Two key implications

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

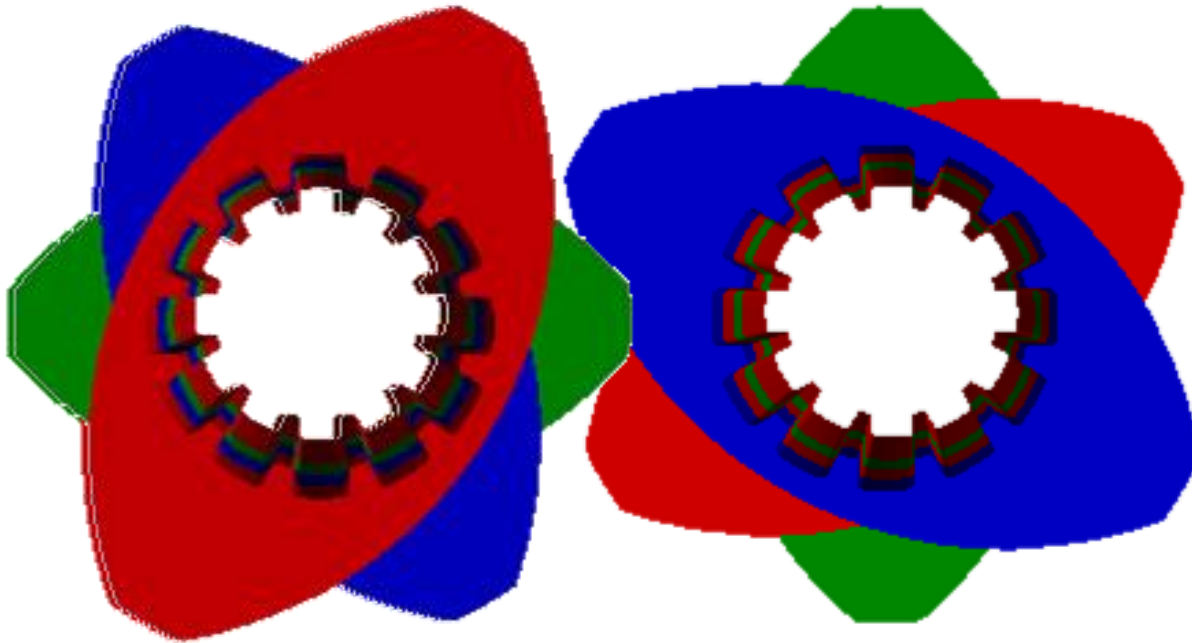


Twin-screw granulation process development

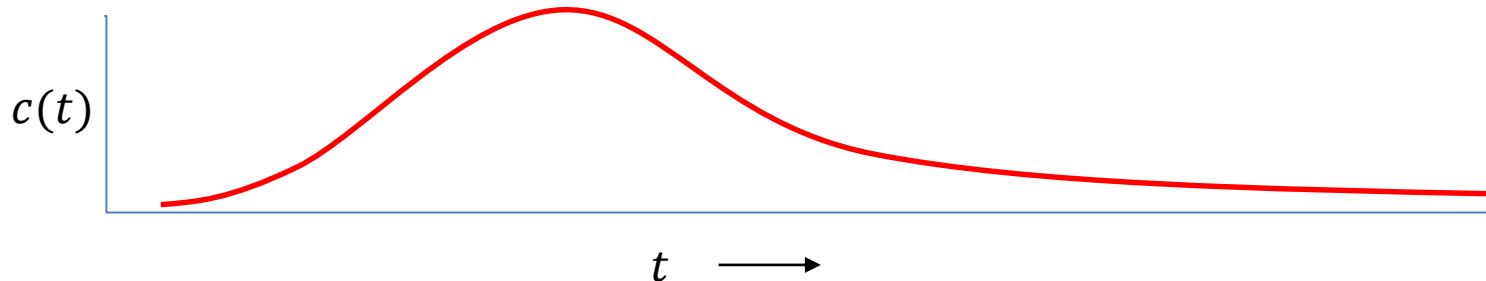
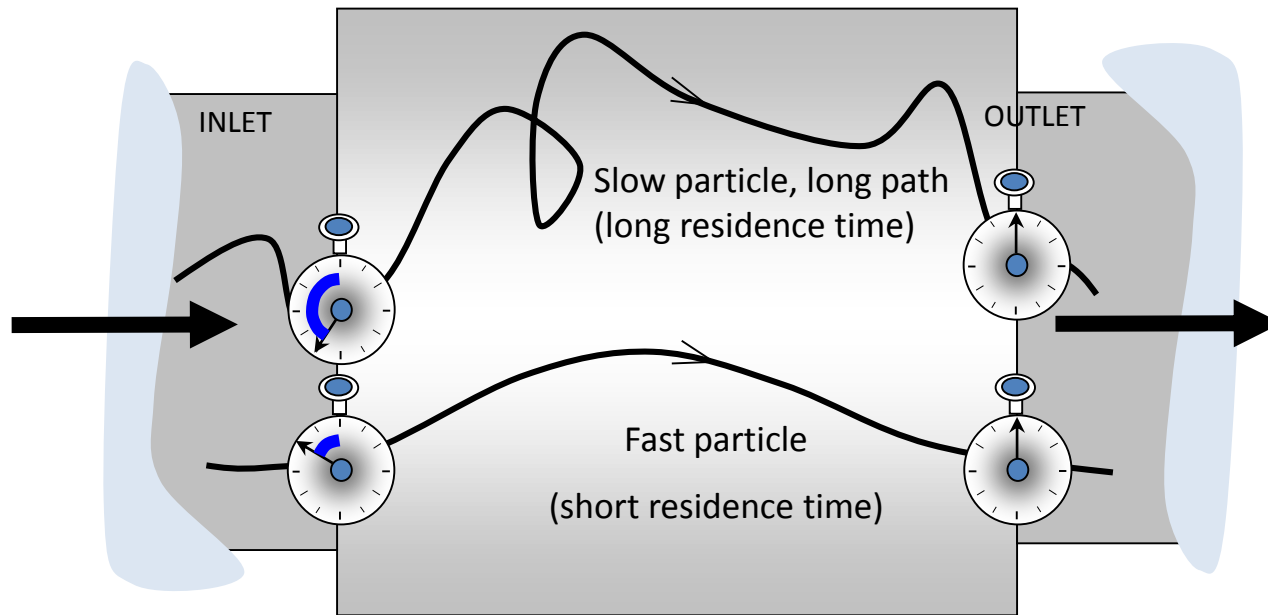
Areas under study:

- Granulation time and mixing.
- Aggregation and breakage rates.

Twin-screw granulation process development



Residence time distribution to know the granulation time and mixing



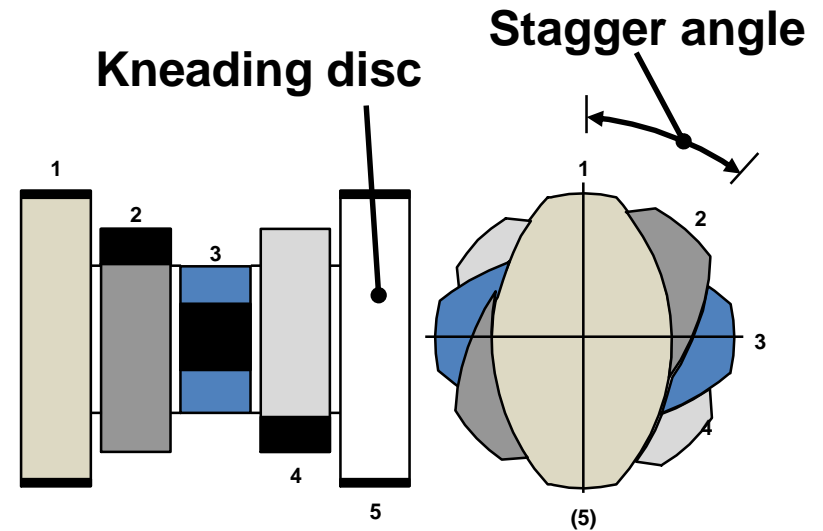
Parameters under study

Screw Configuration

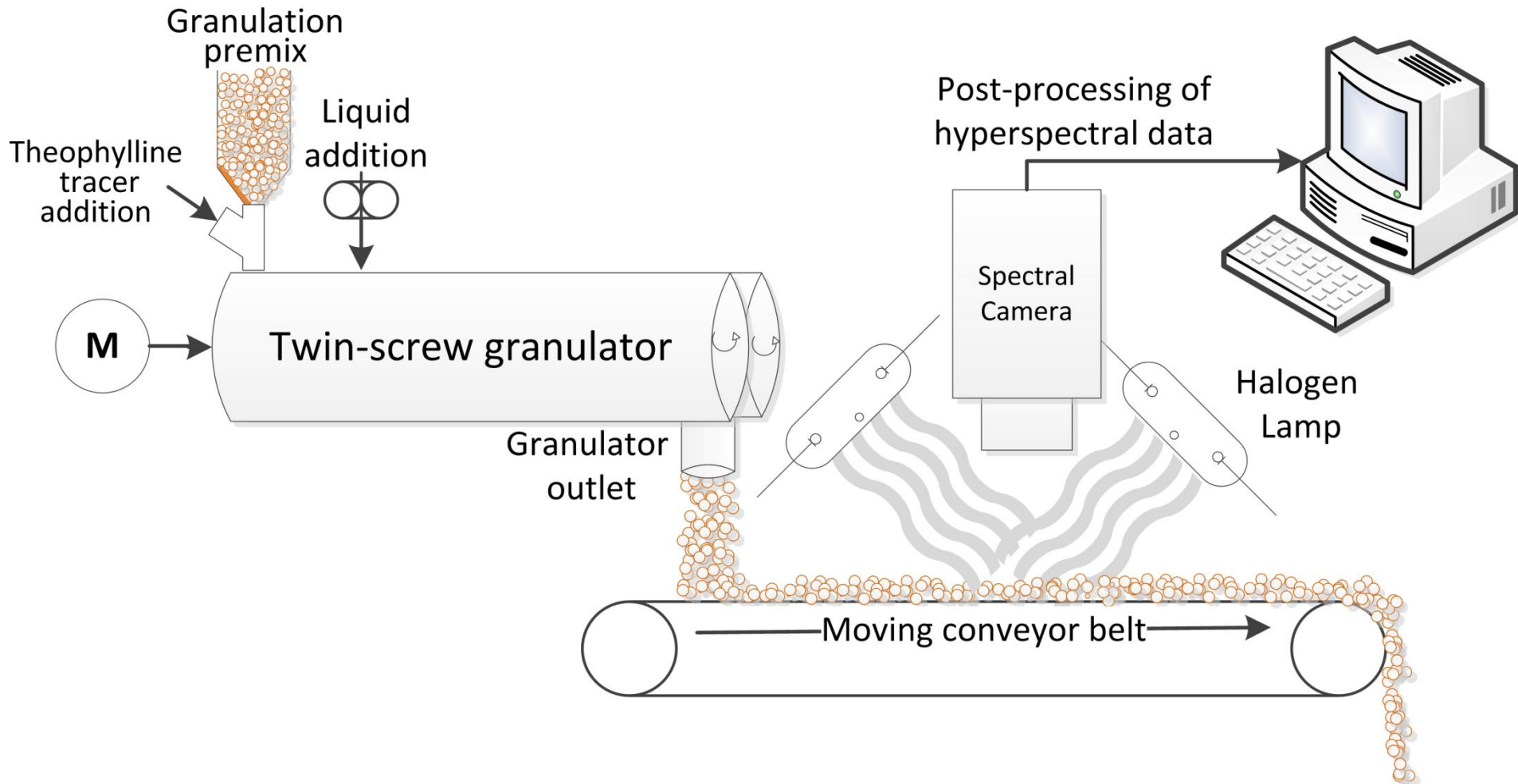
- Number of kneading discs
- Stagger angle

Process settings

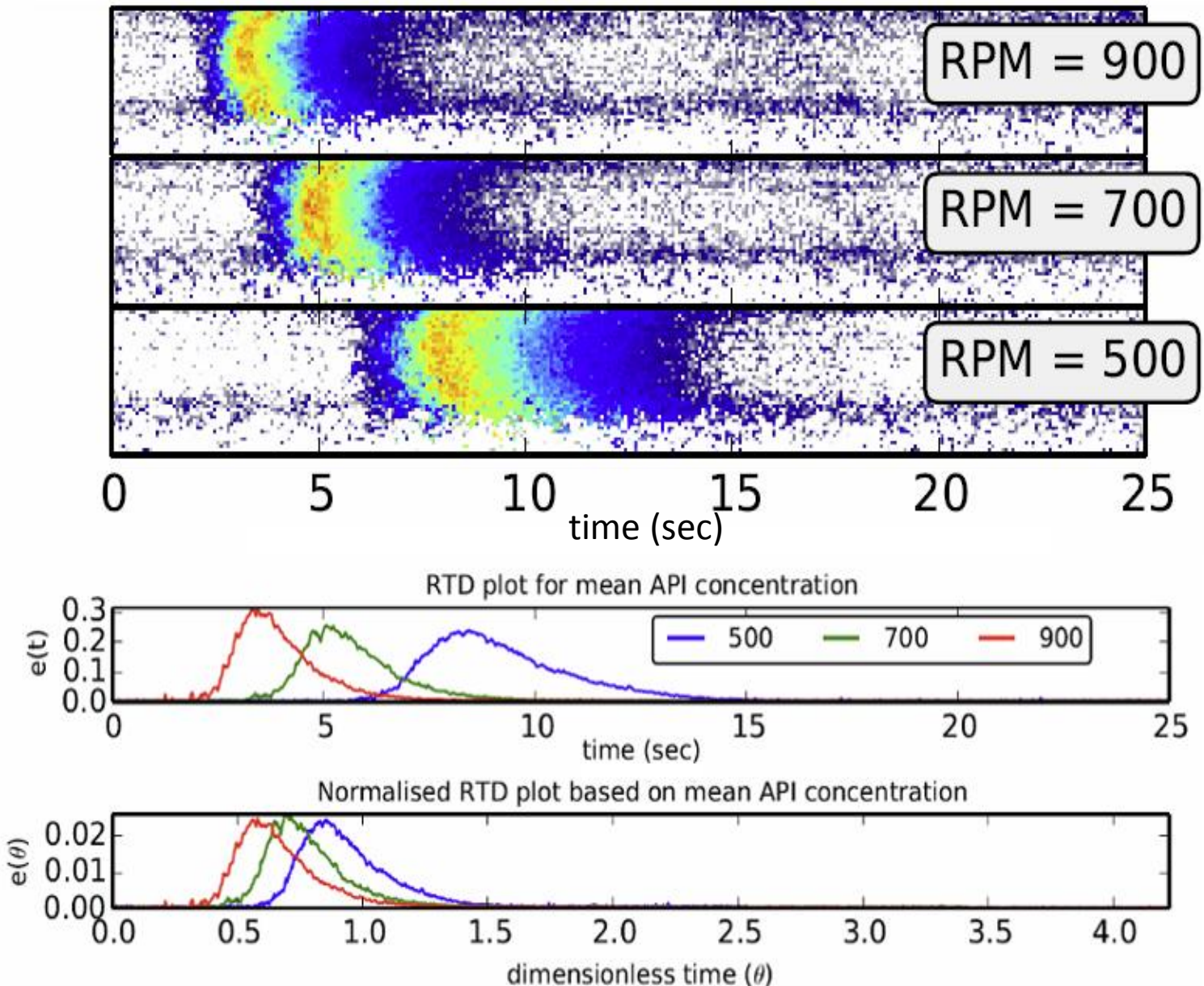
- Material throughput
- Screw speed



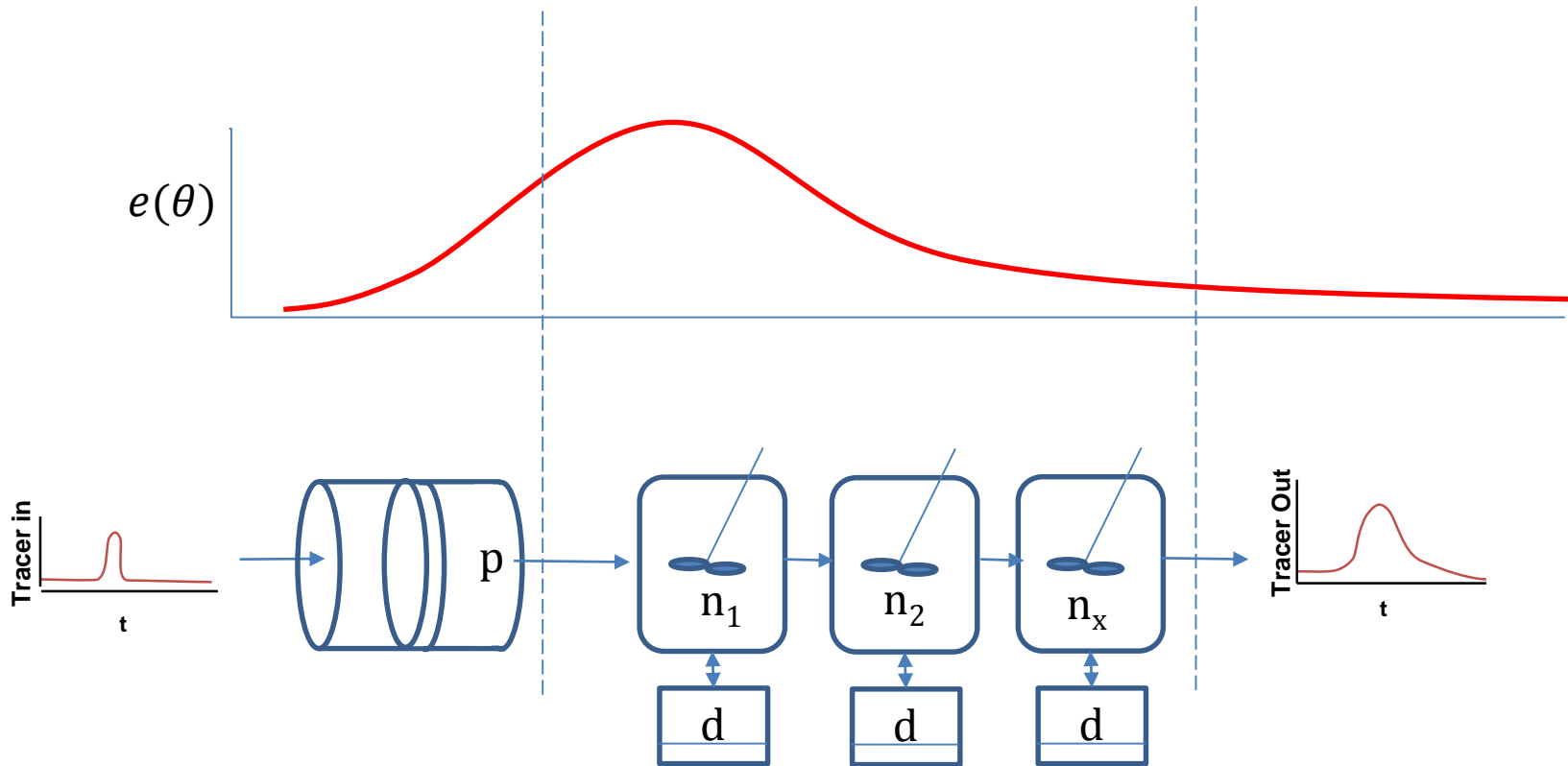
Tracer concentration in granules produced was measured using NIR chemical imaging



API Map was used to measure RTD



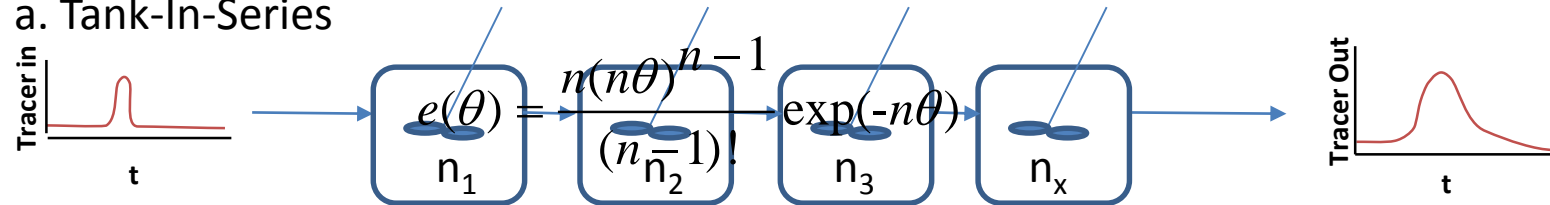
Conceptual modelling for detailed understanding of RTD



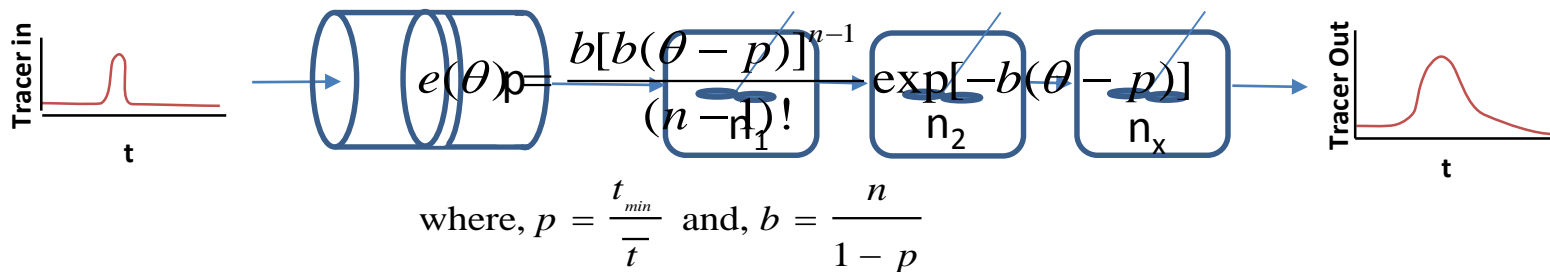
Tank-in-Series model

Conceptual model to include three main components of RTD

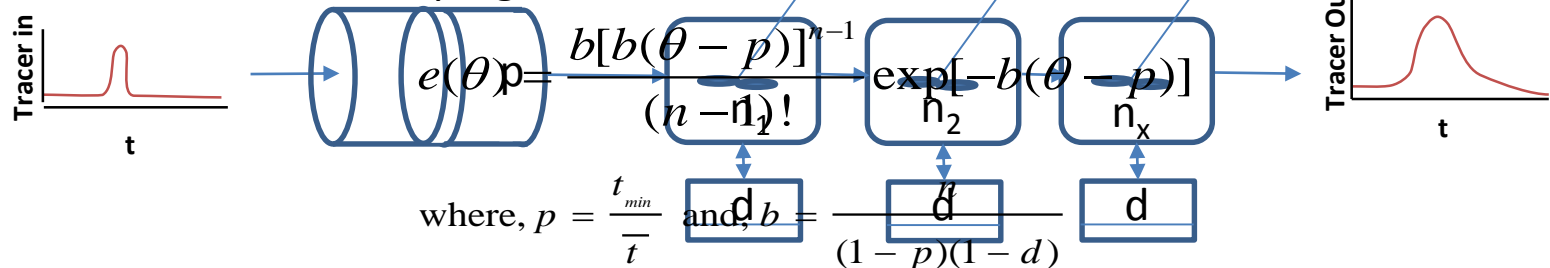
a. Tank-In-Series



b. Tank-In-Series with plug-flow fraction



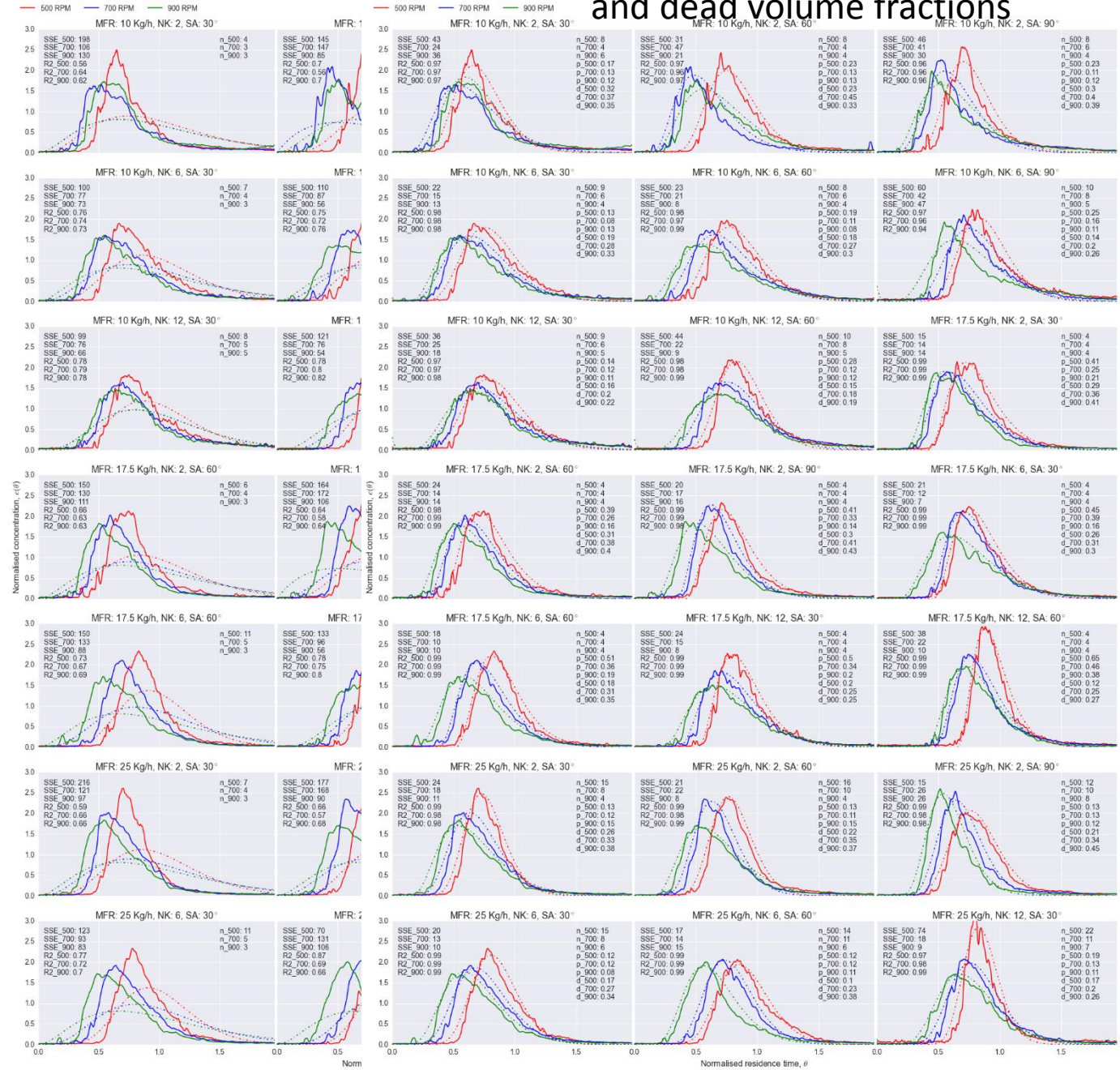
c. Tank-In-Series with plug-flow and dead volume fractions



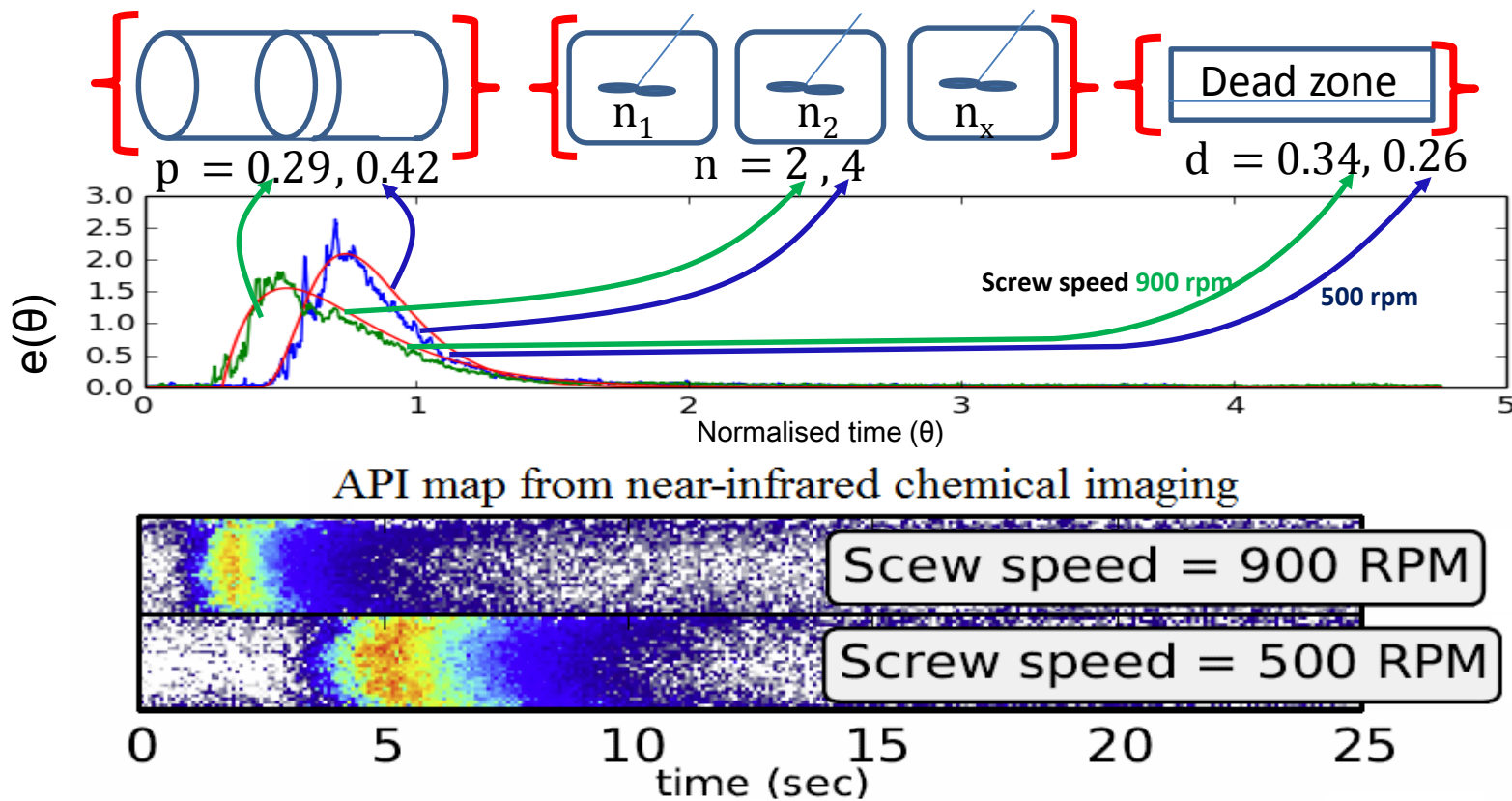
Tank-In-Series

Tank-In-Series with plug flow

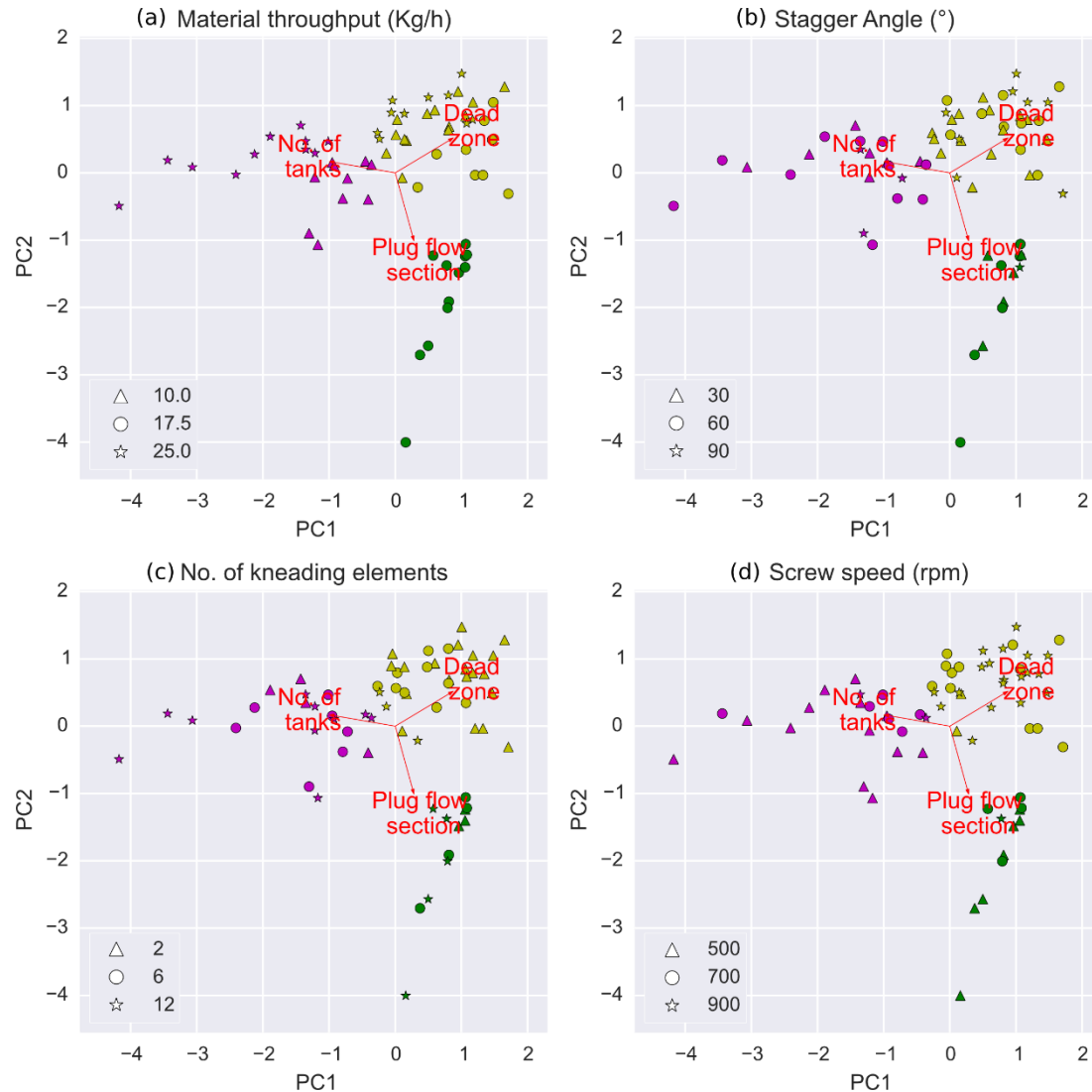
and dead volume fractions



Parameters estimated by the model used for system analysis



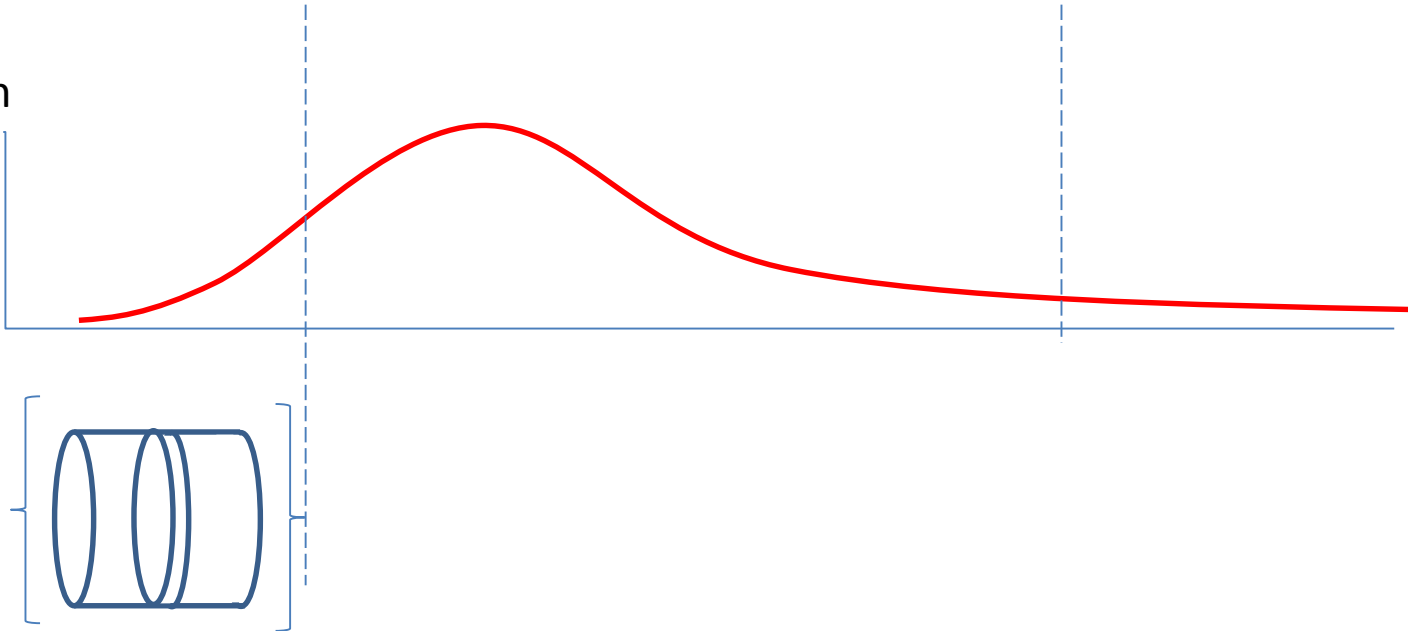
Parameters estimated by the model used for system analysis



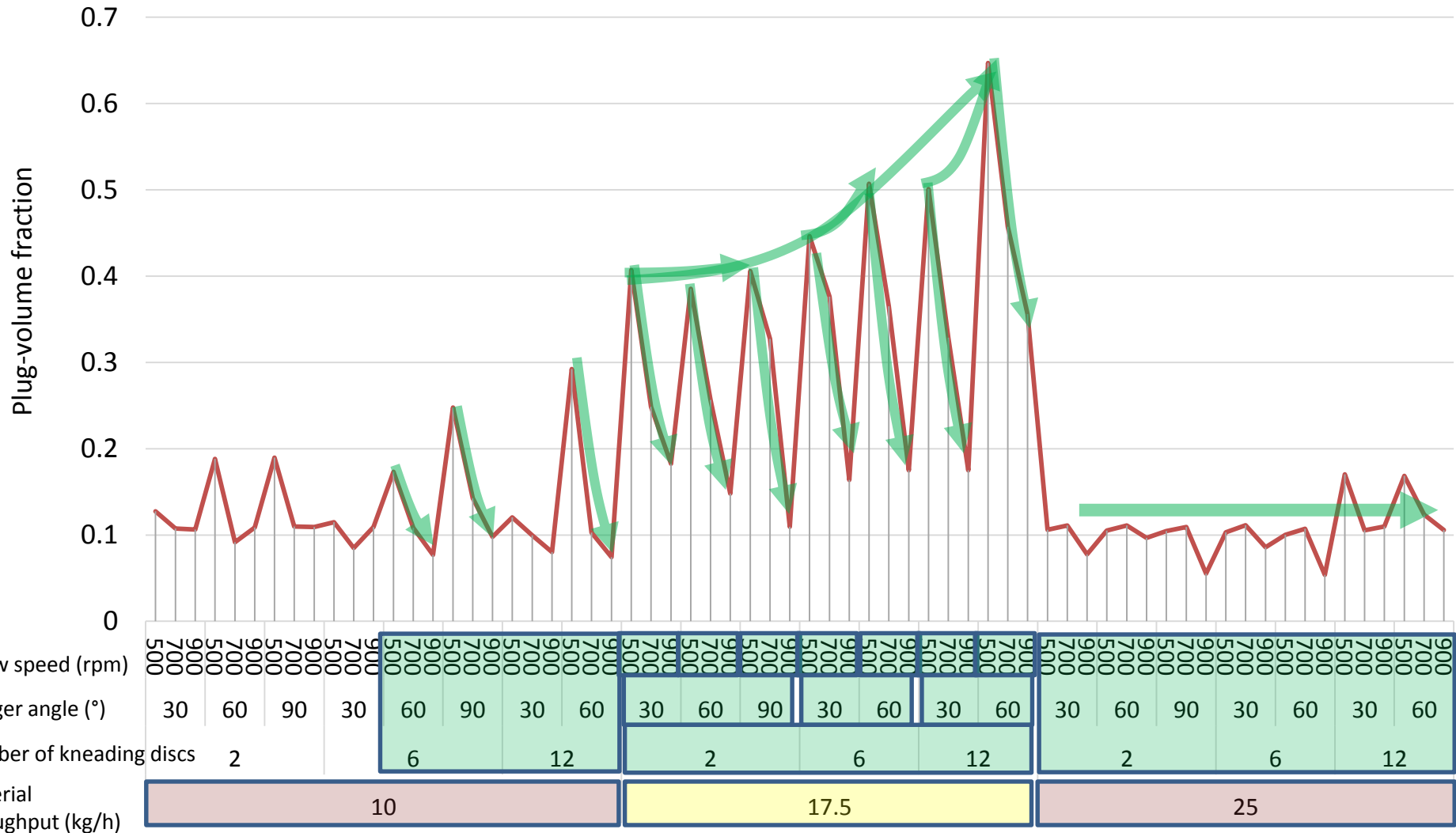
Plug flow component of the RTD

Tracer
addition

$e(\theta)$



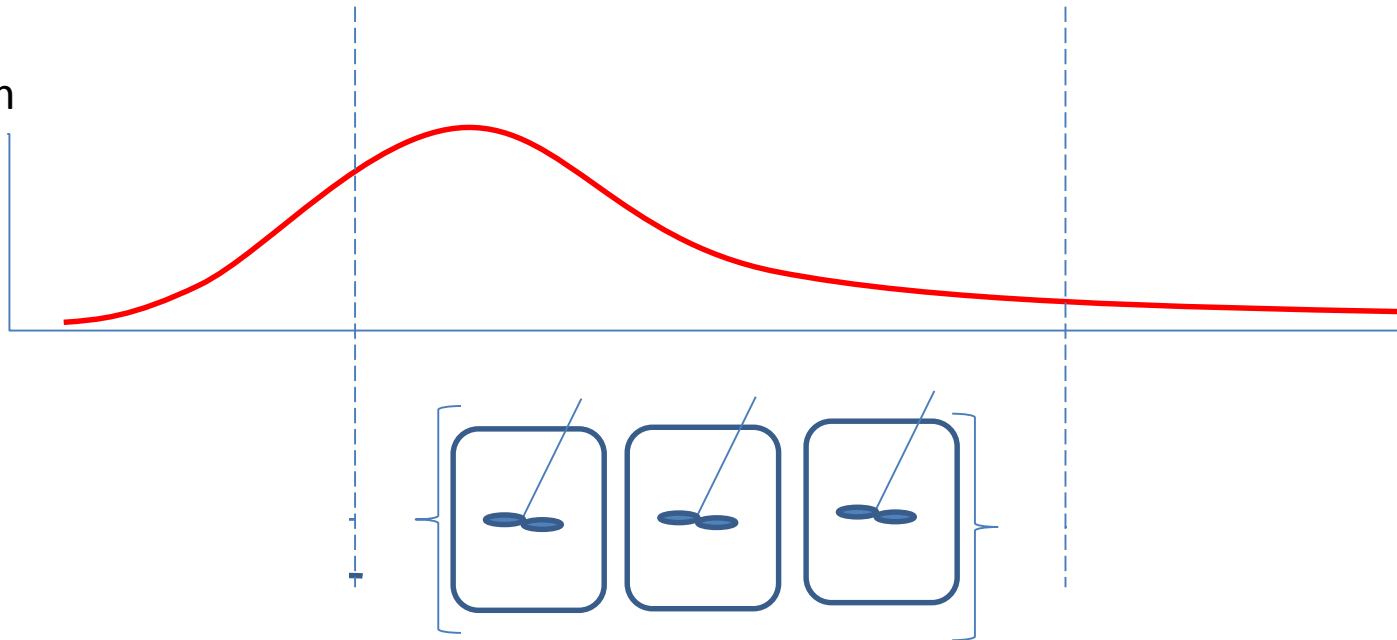
Plug flow fraction decreases with increase in screw speed



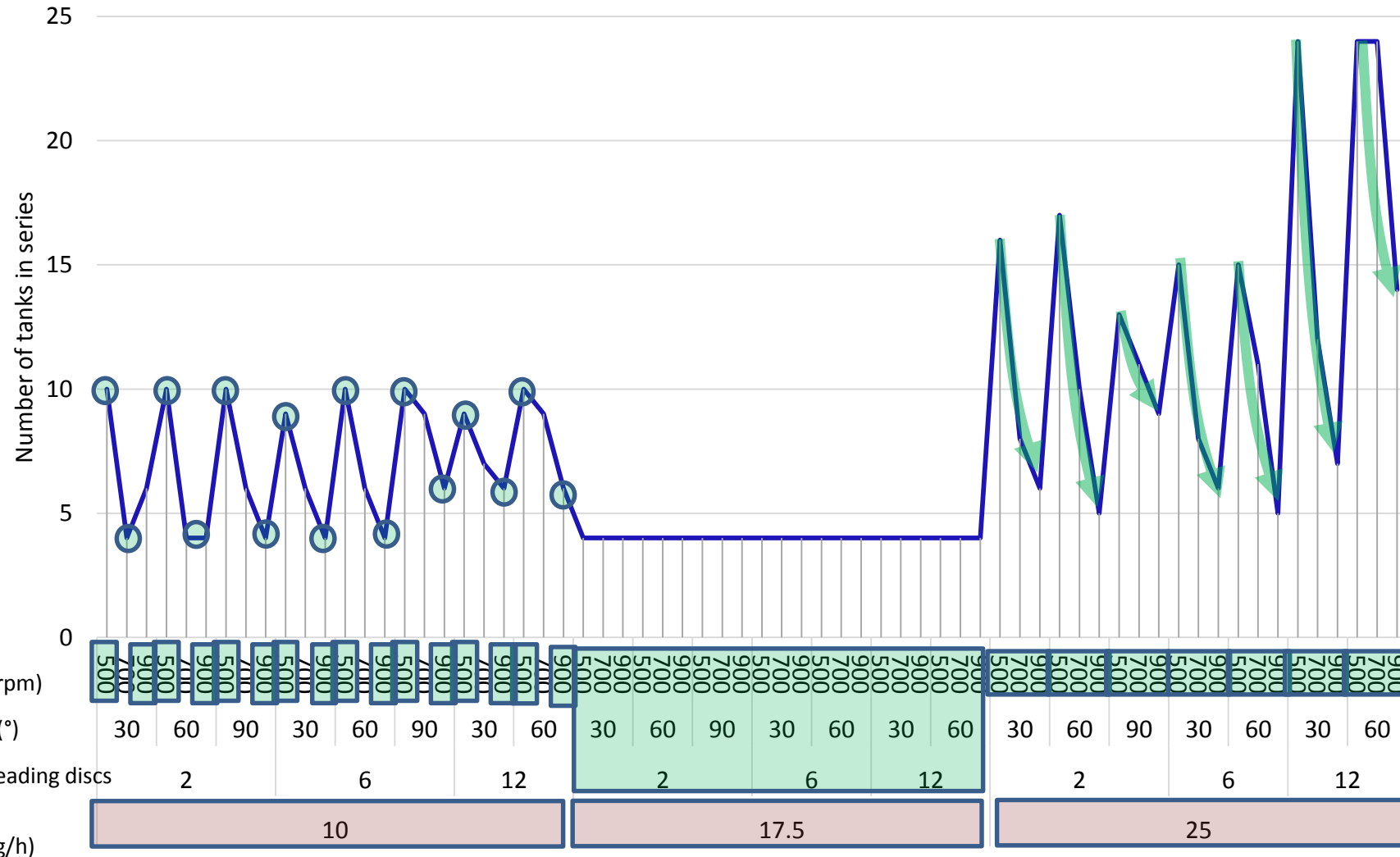
Mixed flow component of the RTD

Tracer
addition

$e(\theta)$



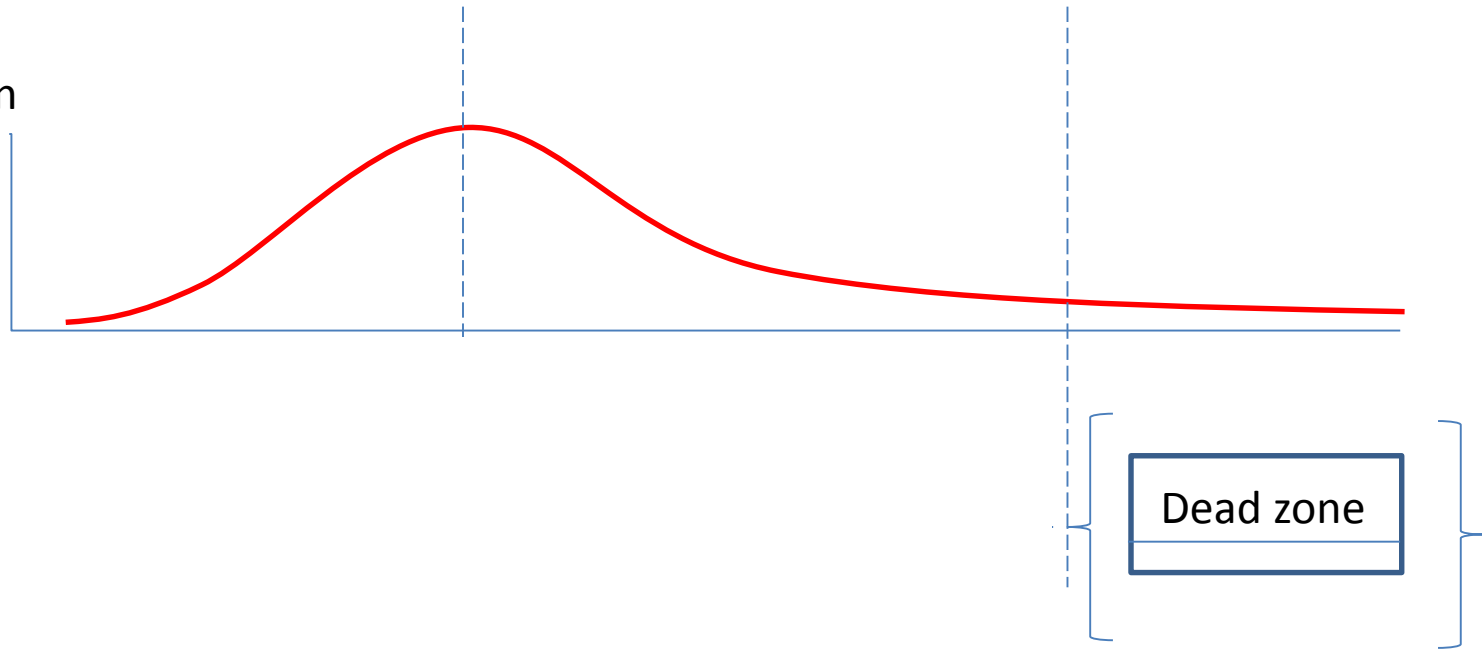
Material throughput controls mixing regime, increase in screw speed increases mixing



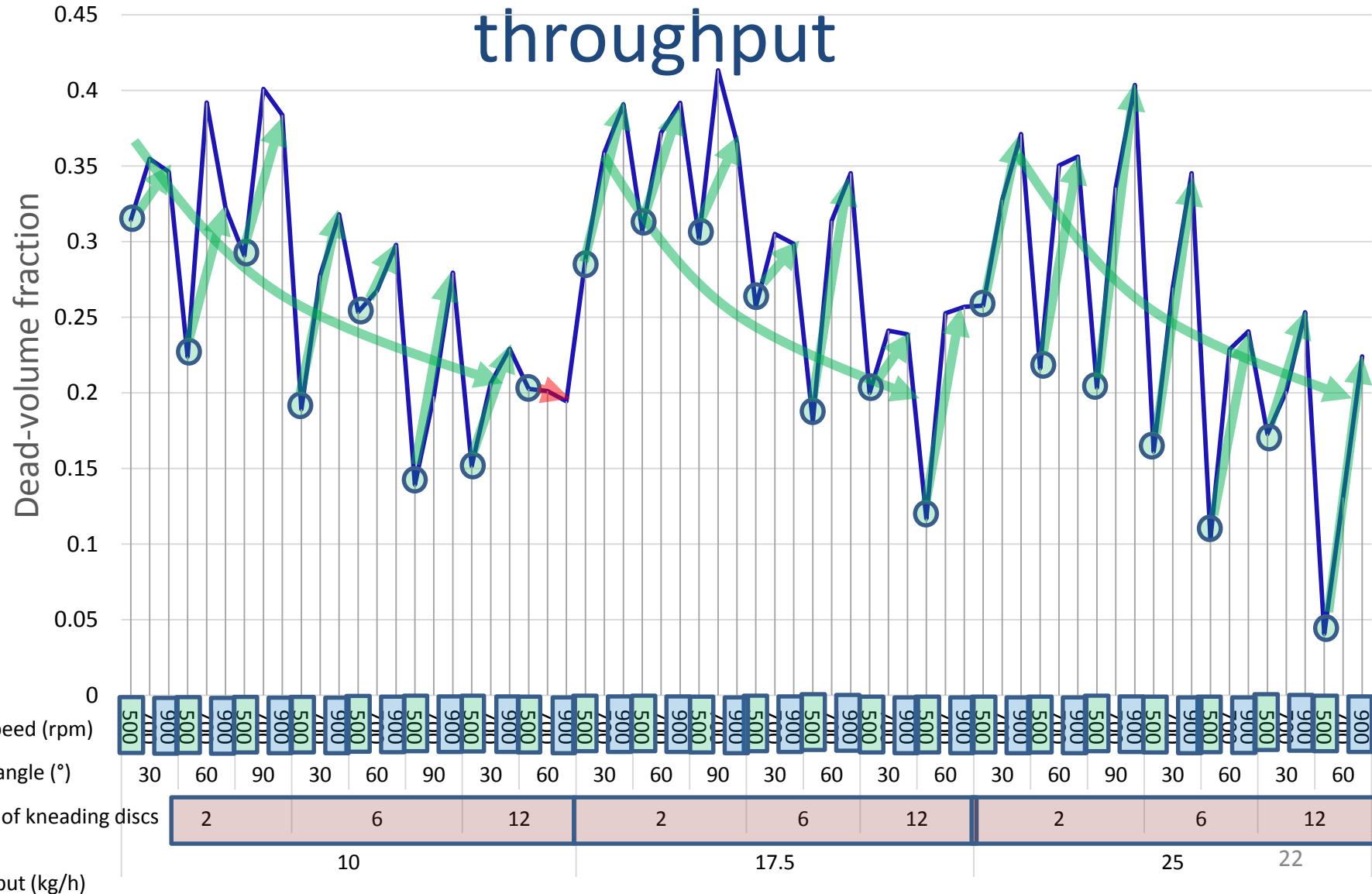
Dead-volume component of the RTD

Tracer
addition

$e(\theta)$



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



Summary and Outlook

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

A **balance between conveying rate and throughput force** is required for good axial mixing.

Kneading block primarily act as plug-flow zones so it also prevent excessive back mixing in the granulator.

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

Aknowledgements

Thomas De Beer
Ingmar Nopens
Krist V. Gernaey



Jurgen Vercruysse
Valérie Vanhoorne

Maunu Toiviainen
Panouillot Pierre-Emmanuel
Mikko Juuti



Kris Schoeters

