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AN EXTENDED 3-COMPARTMENTAL MODEL FOR DESCRIBING STEP-CHANGE EXPERIMENTS IN PHARMACEUTICAL TWIN-SCREW FEEDERS AT DIFFERENT REFILL REGIMES

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Introduction

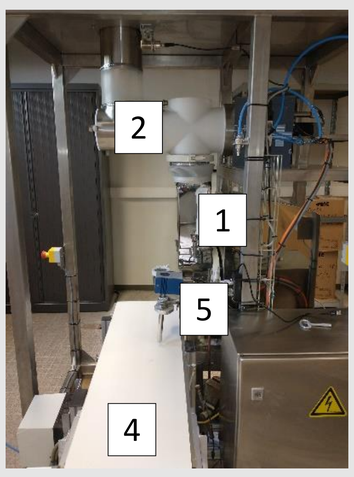
- **Traceability** is an important concept in continuous manufacturing, for which **residence time distributions (RTDs)** are a valuable statistical tool.
- Typically, **tanks-in-series (TIS)** models are fitted to the observed step responses. However, they require the **constant volume assumption** to be valid.

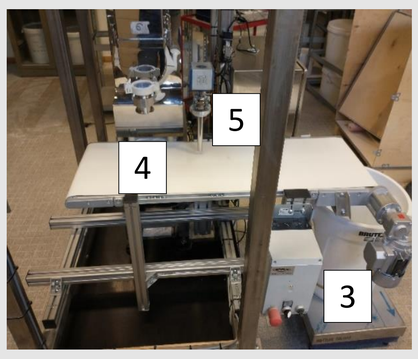
Objectives

- Move away from the constant volume assumption and perform **step-change experiments for different refill regimes**, as refills are typically performed for lower hopper fill levels.
- Develop and validate a **compartmental model** that can explain the observed phenomena for different refill regimes and that increases the **understanding of the internal mixing patterns**.

Materials & methods

- **Experimental set-up: Brabender DDSR20-QR (Brabender Technologie)**



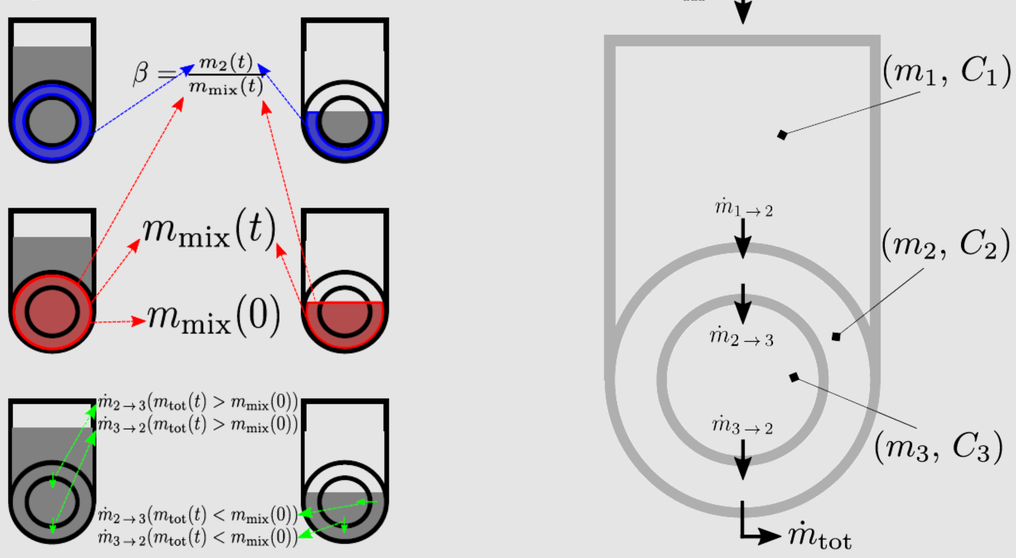


1. LIW-feeder
2. Automatic refill system (FETTE compacting)
3. Catch scale
4. Conveyer belt
5. NIR probe

- **Full factorial experimental design**

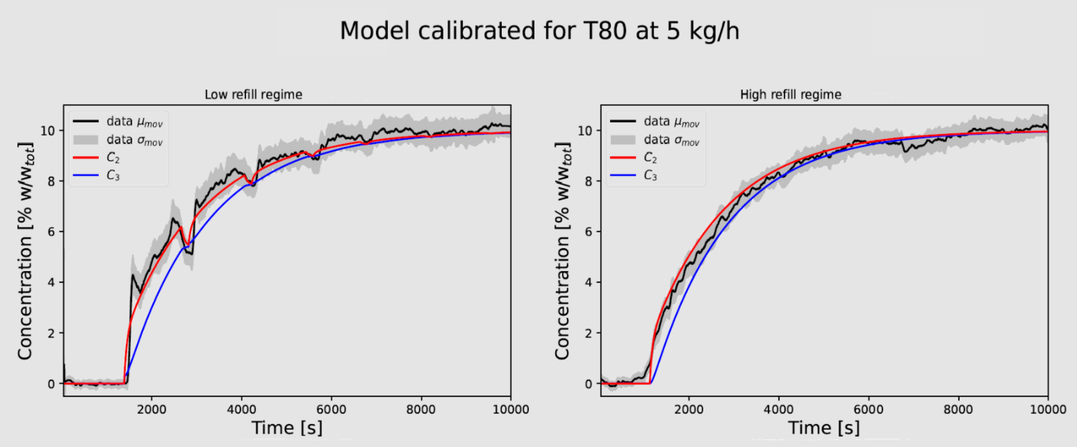
Material	Throughput [kg/h]	Refill regime
Tablettose 80	5	low
Microcelac 100	17,5	mid
Avicel PH-101	30	high

- **Compartmental model**



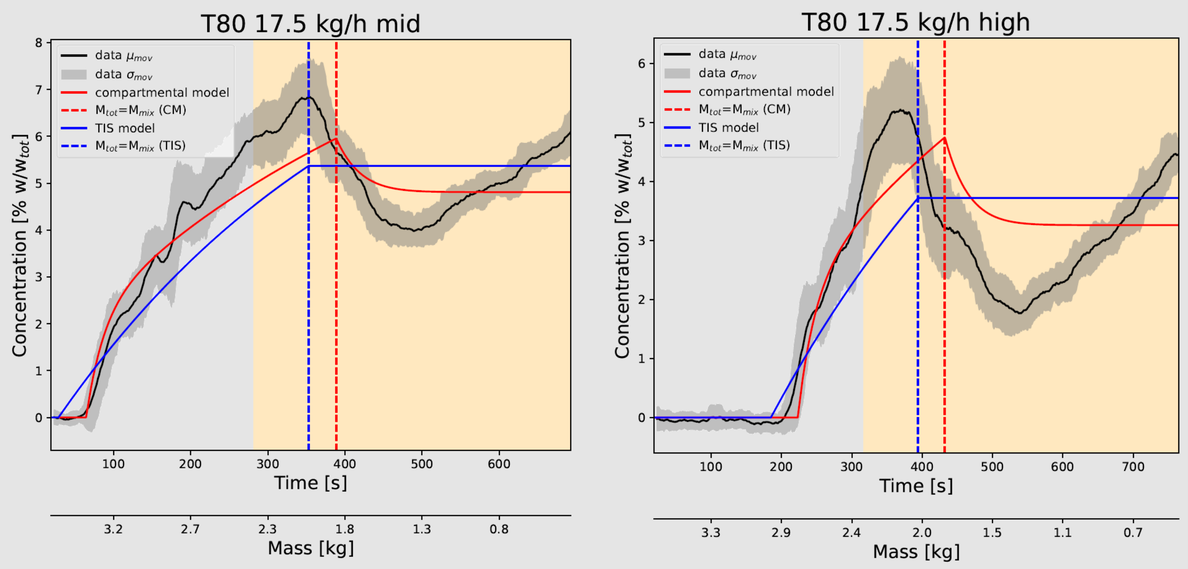
Results

- **Calibration**



Model parameters are simultaneously calibrated for the 3 studied refill regimes.

- **Validation**



The compartmental model shows a steep initial phase and a peak value for the emptying experiment, opposite to the TIS model.

Conclusions

- The **3-compartment model** reliably describes **high and low refill regimes** (e.g. dips at low refill regimes) and shows **transferability** to new situations (e.g. the peak value for emptying experiments).
- More **physics of the mixing dynamics** is captured by the model. Models of increased complexity might be required for **accurate traceability**, within the LIW-feeder and the continuous line as a whole.

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