POSTER 9

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# Wet milling of mefenamic acid for seed generation: model-driven size reduction for maximizing yield

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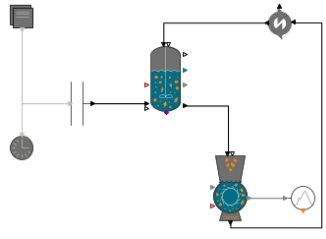
## 1. Introduction

- Wet milling overcomes several common issues encountered with dry milling, including:
  - Undesired polymorphic and amorphous transformations
  - Loss of yield and process control
  - Increased energy cost
- The aim of this work is to explore the region of attainable particle sizes based on the performance of a wet milling model, focusing on:
  - Development of a mechanistic model from initial small-scale experiments
  - Design space exploration to assess the quality attributes and suggest further experimental work with a view to make the model more robust

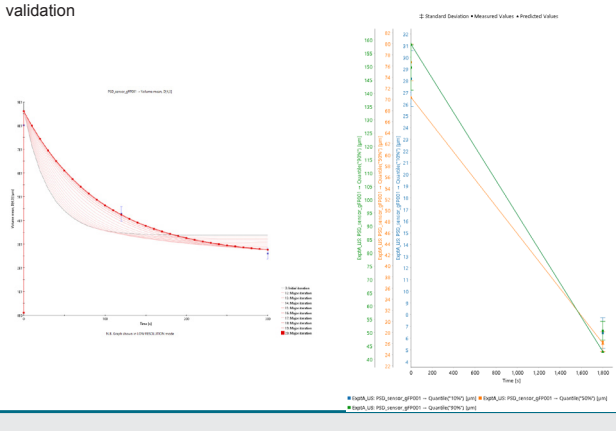
## 2. Mechanistic Model – Wet Mill



- Lab setup included a wet mill in recycle with stirred tank, which was replicated in the model developed using gPROMS FormulatedProducts (gFP)
- Experiments were run with a fine wet mill with 3 rotor-stator rows, and these were used to validate the breakage kinetics

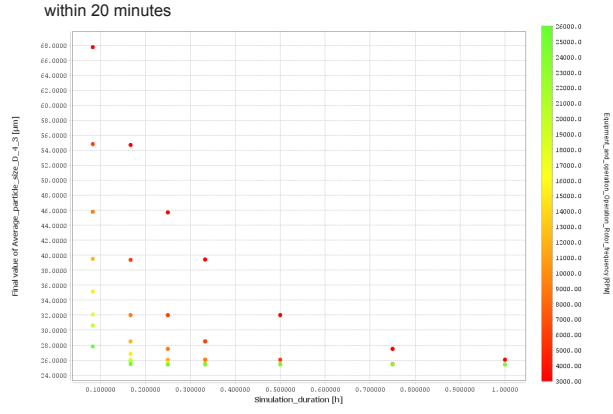
## 3. Parameter Estimation

- Breakage kinetics showed reasonable predictability for end-point particle size distribution, with the predictions being within 10 µm for all quantile measurements
- All experiments used for validation were done with the same mill configuration and very minimal rotation rate differences. A deeper dive into the experimental data showed that this configuration led to very fast breakage rates
- The estimated parameters however were used to explore the design space and suggest further experimental work for better kinetic parameter estimation and validation



## 4. Design Space Exploration

- Two different scenarios were explored in this activity:
  - Different **rotational speeds**
  - Different **rotor configurations (coarse, medium or fine)**
- The results showed that the rotational speed has a great effect on the breakage rate, as expected.
- However, the results were also **able to identify the time when a minimum particle size is reached at different rotational speeds**
  - 3000-9000rpm – gradual decrease in particle size over time, takes up to an hour. Sampling in this range can provide more information on breakage kinetics
  - >9000rpm – rapid decrease in particle size, where minimum size is reached within 20 minutes




  - The model was not able to distinguish between different rotor configurations since it was utilised for initial model validation
  - This information was used to guide further experiments with a coarse mill configuration, in order to get a richer data set and eventually achieve a more robust model and suitable equipment correlation to link breakage kinetics to operating conditions & configuration of the rotor-stator wet mill

## 6. Conclusions & Next Steps

- A mechanistic model was developed using gFP to describe a wet mill-stirred tank recycle set up.
- Model validation within gFP was conducted to estimate relevant breakage kinetics for a fine rotor configuration and varying rotational speeds
- Design space exploration on the validated model showed that the rotor speeds used would have resulted in very fast breakage rates.
- This information has been used to guide further experimental work – at lower rotational speeds and a different rotor configuration – to revalidate the existing model and make it more robust and descriptive of the process behaviour

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