A Process Model for Twin Screw Granulation

Using models to optimise implementation of new technology platforms

A cutting-edge modelling approach can dramatically reduce experimental burden without sacrificing process understanding

Drivers

Twin screw granulation offers a flexible and effective continuous formulation route, but the near-infinite potential variations in screw elements and set-up that provide such useful configurability also make it highly challenging to cover all the options in a solely practically-based approach to platform optimisation.

The purpose of this case study was to see to what extent modelling could be used to reduce the number of practical trials needed without sacrificing the amount of process understanding obtainable across the full range of design space. A lower experimental burden (cost of materials and time spent in experimental design, execution and analysis) equates to increased efficiency in development and cost reduction.

Approach

An early version of an advanced mechanistic model using a population balance based approach to describe the complex set of simultaneous rate processes occurring within a twin screw granulator was implemented within a worksheet environment by PSE for evaluation to see how close it was to utility as part of a normal AZ development workflow.

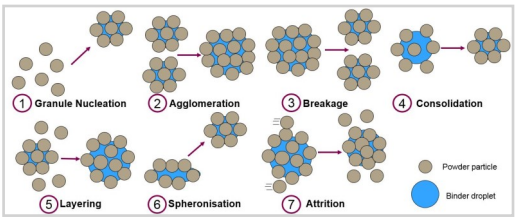
Key Features

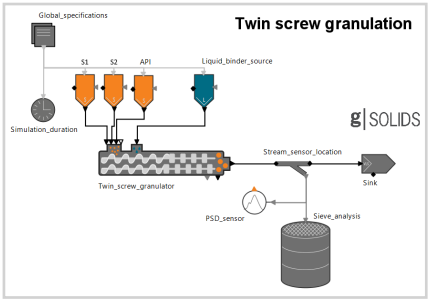
- An advanced mechanistic model has been evaluated in a flowsheet environment facilitating rapid, virtual experimentation in place of expensive and time-consuming practical experimentation
- A sufficiently predictive model was achieved using just 5 trials instead of 24
- The study demonstrates the potential for early, virtual process platform optimisation

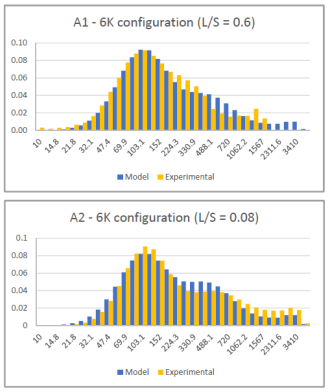
The tool was used on a retrospective example to assess the potential for reduced experimental requirements. Whilst the case study was fairly limited in scope - a practical design space including two screw configurations was used to predict behaviour in a third – a sufficiently successful demonstration would be a significant step forward and a good indicator of future utility in further process understanding work.

An ADDoPT Case Study featuring collaboration between PSE and AZ

Mechanistic Modelling







Many rate processes occur simultaneously during granulation. A population balance model implemented in PSE's gPROMS FormulatedProducts platform has been used to model the changing properties of the granules as the net result of these mechanisms. The model uses a combination of feed material properties (densities, size), equipment set-up (screw configuration and elements), and process settings (solid and liquid feed rates) as inputs and predicts the output granule particle size distribution.

Up to 80% fewer trials were needed to calibrate the predictive model, and similar economy in pilot validation would be expected

Results and Benefits

Use of the modelling tool reduced dramatically the experimental requirements in the system studied. What was previously a 24 trial practical design of experiments needed just 5 trials to build a sufficiently predictive model for use in further work - exploring parameters in a fuller virtual design space, or helping researchers better target further regions of design space likely to be of most interest.

Using the model to conduct sensitivity analysis, the experimenter is directed towards regions of operating space which are (a) most informative in terms of which are the most influential parameters, and (b) most likely to allow production of tablets which can be used to establish if CQAs can be met.

A particular advantage arises if an organisation can model a technology in which it lacks an extensive "platform history" to use as a starting point (as is the case with TSG in AZ). By helping experimentalists reduce a potentially huge parameters space down to something more tractable, substantially more rapid and less costly early stage process design and development may be envisaged.

Further Steps

This case study has provided useful insight into how such a model-based approach could be applied more generally to other relatively new formulation technology platform introductions, such as continuous direct compression. There is growing business recognition that modelling to allow "sparser" experimentation is a necessity to make a success of such technologies because of the prohibitive costs of the required full experimentation.

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