Hyperspectral imaging for continuous process development

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Problem statement

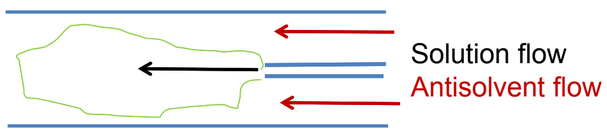
In production of high value chemicals as pharmaceuticals, a strict control over the final product attributes like size, purity, morphology, form etc. is required. Traditionally pharmaceuticals are produced in batch mode where it is not possible to fully control process operation and the final product quality varies from batch to batch. Moving from batch processing to continuous operation offers opportunities for improvement in consistency of the product attributes. However, development of advanced techniques for on-line process monitoring and control is needed.

Using hyperspectral camera

The process is continuous crystalisation of a solute of a pharmaceutical compound using antisolvent in tubular crystalliser. Antisolvent crystallisation is a very rapid process, requiring tight control of enviroment conditions.A feasibility study has confirmed that hyperspectral camera can deliver spatial concentration distribution information not available from other techniques. Hyperspectral images have been acquired to reveal the size and shape of the resulting jet, and relate its properties to the crystals produced.

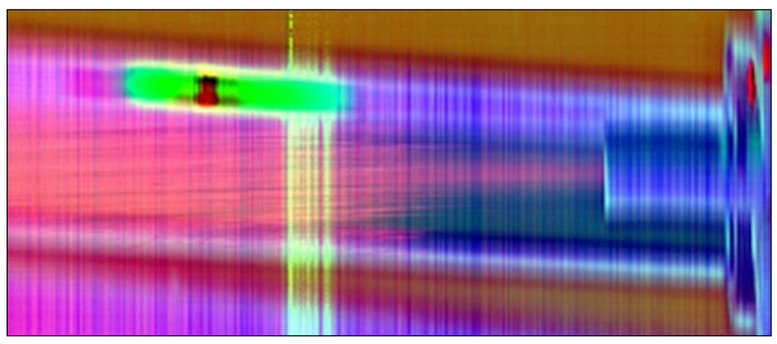
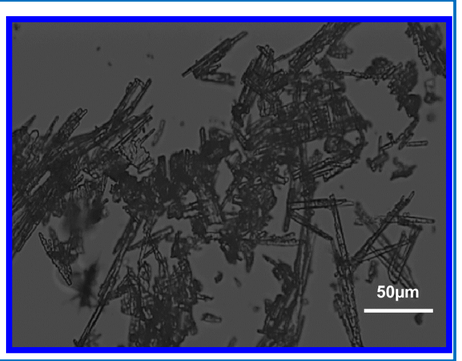
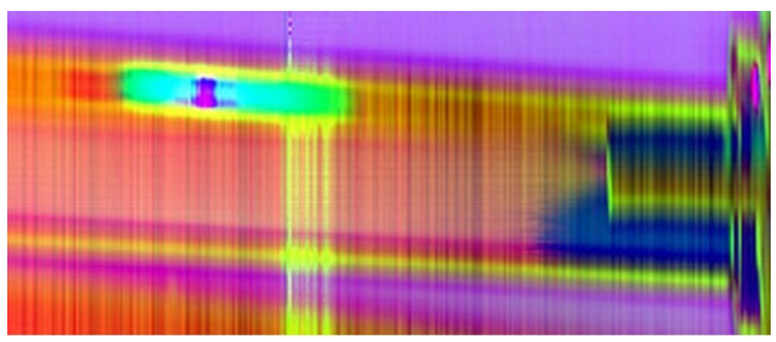
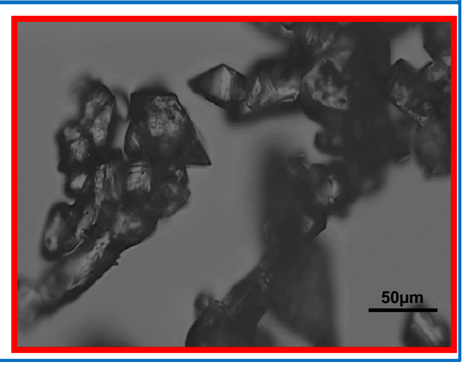
The process is now being upgraded with computer controlled pumps and hyperspectral compatible photo booth, for long term usability and repeatability of further developments.

continuous crystaliser



The solution is continiously introduced into the antisolvent flow using a nozzle in the middle of the vessel. The resulting crystalisation process is very rapid and the product properties (crystal size, shape, aglomeration, amount of product recovered from solution) depend heavily on the shape and size of the jet. Hyperspectral images allow distinction of the two chemical compounds that are otherwise white or transparent to human eye. It is possible to obtain quantitative measurements of the mixing properties.

Feasibility study results

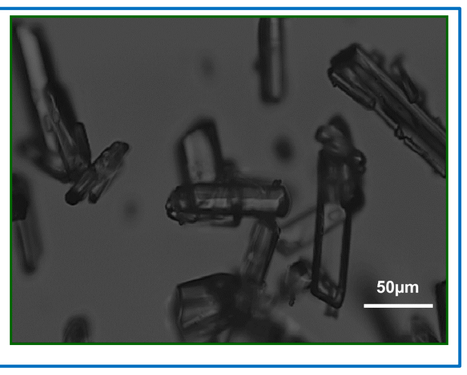
Conditions	– Hyperspectral image	– Product image
Low flow rate Total flow: 100g/min 20g/min solution 80g/min antisolvent d=0.5mm, Re=652, v=1.70m/s Residence time=10sec		
High flow rate Total flow: 200g/min 40g/minsolution 160g/min antisolvent d=0.5mm, Re=1304, v=3.4m/s Residence time=5sec		

Reference batch crystaliser

For comparison, the same pharmaceutical was crystalised in a batch crystaliser. The resulting product is shown in the microscopic image to the right.

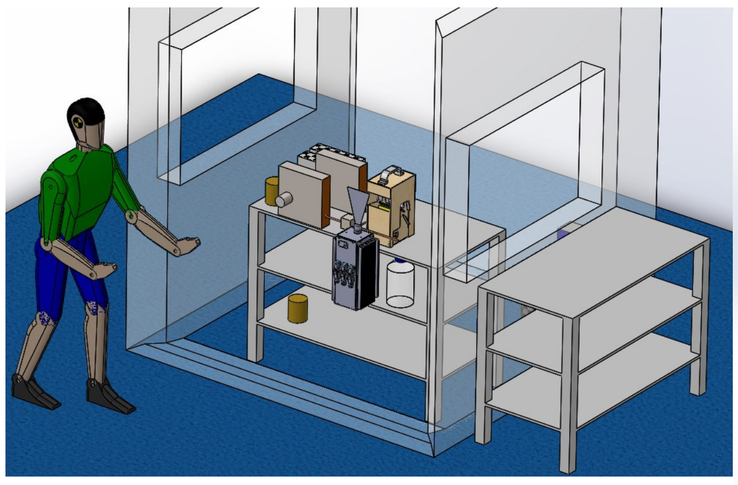
Station type: Mettler Toledo EasyMax

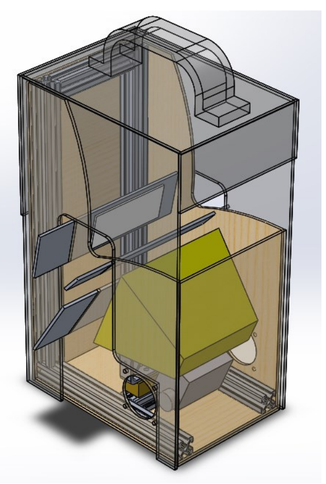
Total volume :100ml
Stir rate: 400rpm,
Cooling: 1°C/min



New experimental setup

The experimental setup is being upgraded to support long term automated experiments with parametric sweeps of flow concentrations, and tighter control of image acquisition parameters.





Experiment automation

A parameter sweep, covering a range of input variables like temperature gradients, flow rate, mixing ratio, e.t.c. can be programmed into the controller to perform a comprehensive study of the system behaviour. Data is carried over local OPC hub and stored in database for easy retireival into the electronic lab notebook.

A holistic approach is used to design the experimental booth. The path of the light from the source, through the specimen, to the camera, has been optimized for final image quality.

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